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# THE AMERICAN SURGEON

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## THE SURGICAL SIGNIFICANCE OF TUMORS IN IDENTICAL TWINS\*

A SHORT REVIEW OF THE LITERATURE AND A REPORT OF  
SYMPATHICOBLASTOMA OCCURRING IN MONOZYGOTIC TWINS

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*Cincinnati, Ohio*

The occurrence of tumors in identical twins is a subject which has interested geneticists and oncologists for a number of years, but it has not received very much attention in the surgical literature. While the average surgeon may not frequently encounter such a situation, it is important that he be aware of its implications. When a tumor, especially a malignant tumor, is recognized in one of identical twins, there is considerable possibility that a malignant lesion, usually, but not always, of a similar type, will appear in the other twin. The purpose here is to review the evidence supporting this thesis and to record what is believed to be the first reported instance of sympathicoblastoma occurring in both members of identical twins.

The subject of twins, both identical or monozygotic and fraternal or dizygotic, has been extensively investigated by students of genetics. The recent comprehensive review of Bronson Price<sup>12</sup> and the monograph of Newman, Freeman, and Holzinger<sup>9</sup> provide abundant source material on this phase of the subject. For the present purpose it is sufficient to state that fraternal or dizygotic twins have nothing more in common, from a genetic or developmental standpoint, than do ordinary siblings. They are no more susceptible to identical congenital defects or to the development of tumors than are brothers and sisters who do not happen to be born twins. Identical, or monozygotic twins, on the other hand, very com-

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monly have identical or mirror-image congenital defects and the tumor diathesis in one is very likely to be present in the other.

According to the most recent available vital statistics,<sup>15</sup> there are about 37,500 twin births in the United States each year. Approximately 25 per cent of all twins are monozygous, which means that approximately 9,375 pairs of identical twins are born in the United States each year. It can be seen that the total identical twin population is large enough to merit consideration from the standpoint of cancer control.

One of the earliest comprehensive studies of this subject was that of McFarland and Meade, in 1932, entitled "The Genetic Origin of Tumors Supported by Their Simultaneous and Symmetrical Occurrence in Homologous Twins."<sup>7</sup> These authors reviewed the literature extensively and list the case reports of both congenital anomalies and tumors common to both individuals of monozygotic twins. Their list of tumors includes chondrous exostoses, medulloblastoma, glioma, adenofibroma and carcinoma of the breast, melanoma and retinoblastoma of the eye, congenital cystic tumors of the kidney, papilloma of the larynx, carcinoma and cystoma of the ovary, nevi of the skin, testicular sarcoma, and myoma and adenocarcinoma of the uterus. There is no mention of sympathicoblastoma. In a later publication<sup>8</sup> McFarland further discusses the genetic factors, and mentions an instance of fatal melanoma in one twin while the other, at the time of writing, remained healthy.

Macklin<sup>6</sup> reports a number of instances of malignant tumors, not always of identical type, in identical twins. In one of her cases the first twin had a medulloblastoma of the cerebellum and the other a sarcoma of the scapula, both occurring at the age of 14 years. She describes gastric carcinoma occurring in both twins at the age of 47 years, and adds several examples of cases similar to but not included in McFarland's reports. Again there is no mention of sympathicoblastoma. Fister<sup>2</sup> records an instance of carcinoma of the prostate simultaneously occurring in identical twins at the age of 68 years and Stocking<sup>14</sup> describes carcinoma of the cervix in identical twin sisters. In Granet's<sup>4</sup> cases a benign lymphoma of the rectum was found in one twin at the age of 31 years and an identical lesion was found in the other seven years later at the age of 38 years. A similar situation was observed by Palmer and Mitchell<sup>10</sup> where adenocarcinoma of the fundus uteri appeared in one twin at the age of 50 years and in the other at the age of 55 years. Both were successfully treated with radium therapy, followed by hysterectomy. Wyatt and Goldenberg<sup>16</sup> encountered multiple polyposis of the colon in 26 year old male twins, believed to be identical, whose father had died of "cancer of the stomach or bowel." Both twins developed carcinoma of the bowel and died within three months of each other although the interval between diagnosis and death was five years in 1 case and three months in the other. Phillips<sup>11</sup> observed adenocarcinoma of the right breast in one identical twin and of the left breast in the other, the tumors developing three years apart.

Gaulin<sup>3</sup> recently reported simultaneous Wilms' tumors in 15 month old male identical twins. Both infants were admitted to the hospital the same day. One

succumbed to surgical removal of a tumor of the left kidney which weighed 2 pounds, 2 ounces. His brother survived removal of a 2-pound tumor of the right kidney, but died of recurrence three months later.

A reasonably thorough review of the literature has revealed only one instance of sympathicoblastoma in identical twins. Brody<sup>1</sup> reports such a tumor in one of twin girls, the affected twin dying on her fourth day of life. There was considerable doubt as to whether these twins actually were monozygotic. The unaffected sister was living and well 14 years later, when the case was reported. This would be remarkable if the girls were, in fact, identical twins, but since Brody himself is skeptical, it seems more probable that they were not. As has been previously noted, the chance of a dizygotic twin remaining healthy under these circumstances is about as great as it is for a sister who is not a twin.

There are many reports of tumors occurring in fraternal or dizygotic twins, but there is no detectable pattern in either the types of the tumors or in the time of onset, and various analysts have shown that the incidence is no greater than it is in ordinary siblings. However, the foregoing brief review of the literature on tumors in identical twins indicates that their concurrence is much more than coincidental. As Macklin<sup>5</sup> points out, "—tumors affect both members of monozygous twins far more frequently than they do both members of dizygous twins. The tumor is of the same type and occurs in the same organs far more frequently in the identical group than in the nonidentical group. Further, the age of onset is more nearly the same in the former group."

Macklin was interested in the problem from the standpoint of heredity, but the implication to the clinical surgeon is obvious. When a tumor is found in one of a pair of twins, believed to be monozygotic, it is the duty of the surgeon to make an insistent recommendation for the careful examination of the other twin in view of the possibility that a tumor may be found in the second member. Even if it is not, the healthy twin should have repeated careful examinations at regular intervals for the rest of his life, since he stands a much greater chance of developing a tumor than does the average person. Being forewarned, he may be fortunate enough to have it discovered in an early and curable stage. This happy result cannot, of course, always be achieved. Sometimes the tumor is of such a type and in such location that circumstances may prevent the most alert clinician from saving the life of either twin.

The following example is presented because, so far as can be determined from the available literature, there has been no previous report of sympathicoblastoma occurring simultaneously in both members of monozygotic twins.

#### COMBINED CASE REPORT

Twin A, B. P., Twin B, D. P. Birth date July 29, 1951. These Negro male monozygous twins were born at term, by spontaneous delivery in a nearby hospital, and appeared to be normal at birth.

Twin A was first seen in the Surgical Clinic at the Children's Hospital on Sept. 26, 1951 and his brother on Oct. 10, 1951. Both were found to have moderately large right inguinal hernias and questionable smaller inguinal hernias on the left. Both of the larger hernias

were easily reducible and it was recommended that repair be delayed until the infants were older. General examination of both twins was otherwise not remarkable.

Twin B was seen in the Medical Clinic on Nov. 29, 1951 at the age of 4 months. At this time the infant appeared generally healthy, but a mass was discovered in the left flank and the liver margin was palpable 3 cm. below the right costal margin. The infant was admitted to the Children's Hospital on Dec. 8, 1951, and excretory urograms on Dec. 11 showed enlargement of the left kidney and displacement and distortion of the renal pelvis and ureter. Roentgenographic studies of the chest, skull, and long bones were negative.



FIG. 1. Photograph of both twins, taken four weeks after the operation on Twin A (left) and 10 weeks after operation on Twin B (right). The metastatic tumor nodules in the temporofrontal region are clearly seen in both infants. Twin B has a unilateral exophthalmos on the left. The left facial palsy in Twin A is not so well demonstrated, but was present when the photograph was made. The radiation reaction in Twin B is easily recognized. The skin markings in Twin A are residual from the surgical dressing. This twin received no irradiation.

With a preoperative diagnosis of sympathicoblastoma or Wilms' tumor, operation was done on Dec. 12, 1951. The liver was found to contain metastases, but the primary tumor in the region of the left kidney appeared to be resectable and was removed, along with the kidney. Microscopic examination showed a sympathicoblastoma (fig. 2), with a metastatic implant in the kidney.

Because of the clinical and roentgenographic findings in Twin B, his brother was admitted to the hospital on December 11 for study. Although he appeared generally healthy, Twin A's liver was found to be palpable down to the right iliac crest, and a questionable mass was felt in the left upper quadrant. Excretory urograms and chest, skull and long bone roentgenograms were negative. After the diagnosis of sympathicoblastoma was confirmed at operation in Twin B, laparotomy was advised in Twin A, but was refused by the mother. Twin A was allowed to go home while roentgenotherapy was begun on Twin B.

Twin B received 25 roentgen ray treatments over a period of seven weeks, to a total of 4,000 r. Considerable reaction was encountered, with vomiting and anorexia, necessitating

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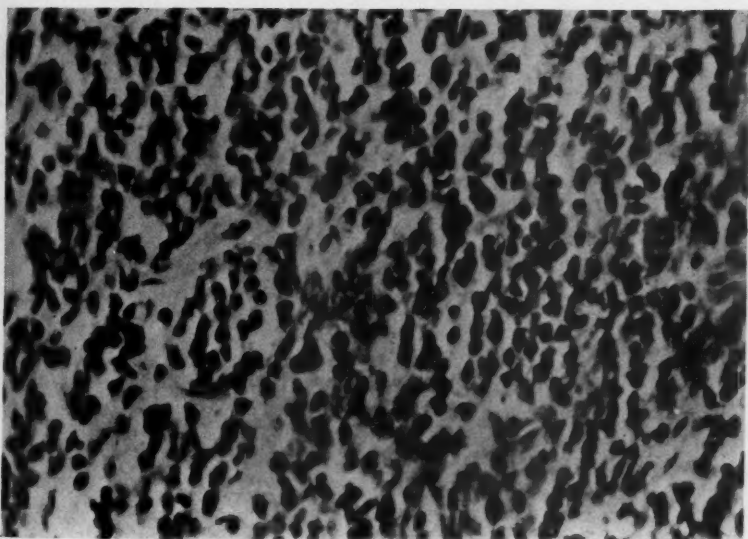
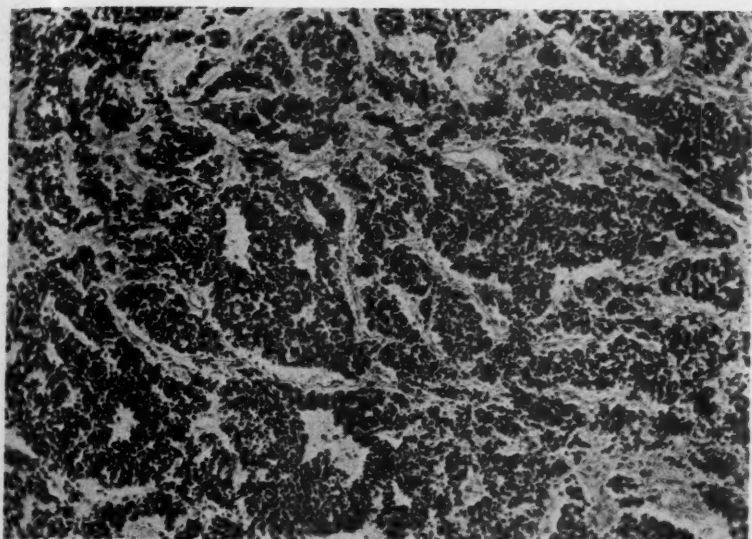


FIG. 2. Photomicrographs of the tumor in Twin B, who was operated upon first. The highly cellular structure of the tumor is shown, with a tendency to form ovoid and irregular groups of cells. Under higher magnification the nuclei resemble those of lymphocytes. There is pleomorphism and hyperchromatism, with only rare mitotic figures. The fibrillary processes are not well demonstrated, but there is an occasional attempt at pseudorosette formation. Diagnosis: Sympathicoblastoma. A is  $\times 160$ —B is  $\times 650$ .



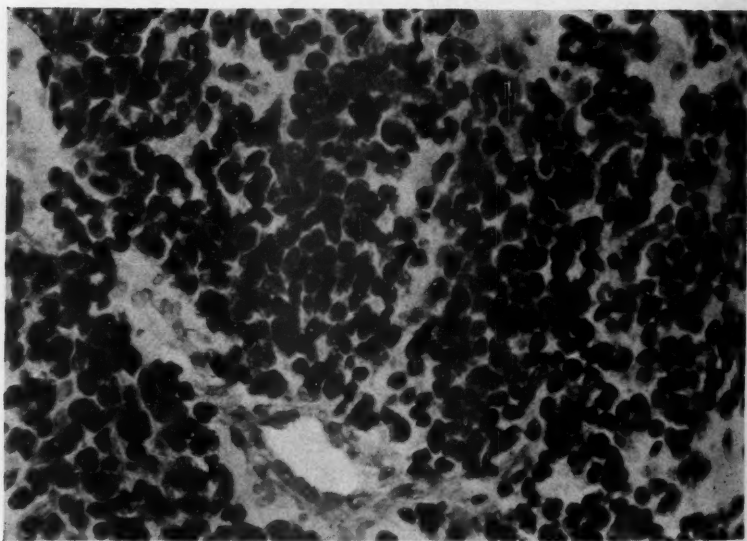
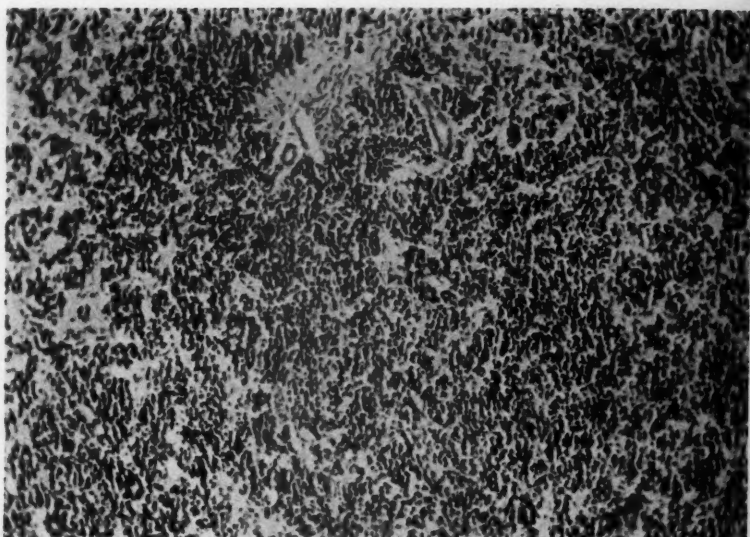


FIG. 3. Photomicrographs of the tumor in Twin A, who was operated upon last. The pattern is similar to that demonstrated in Figure 2, but the classical features are not as well defined. Under high magnification the cells appear to be identical in their morphology but show even less tendency toward a characteristic pattern. Diagnosis: Sympathicoblastoma. A is  $\times 160$ —B is  $\times 650$ .



intermittent parenteral fluid and electrolyte therapy. On January 11 a left subconjunctival hemorrhage was noted and a mass was discovered in the left temporofrontal region near the orbit. Roentgenograms showed metastatic lesions in the left frontal and parietal bones and early signs of increased intracranial pressure. There were no neurological signs other than the vomiting, which was attributed to radiation reaction.

Meanwhile Twin A appeared to be doing well at home and gained weight normally. On December 31 the mother observed a *lump* in the skull near his left eye and on January 6 she noticed that his face was *drawn to the right*. She did not bring him in for examination until January 9, two days before cranial metastases were noted in his brother. A mass was noted near the right orbit and a definite left facial paralysis was present (fig. 1). Skull roentgenograms showed a presumed metastatic lesion in the right temporal region and the liver margin was demonstrated at the right iliac crest both clinically and by flat roentgenogram of the abdomen. With some difficulty permission finally was obtained to remove a biopsy section from the right temporal mass and to do an exploratory laparotomy. Both operations on Twin A were done on Jan. 24, 1952. The liver was found to be filled with metastases in both the right and left lobes. The primary tumor was in the right adrenal with extension into the kidney and the roots of the mesenteries.

The abdominal biopsies as well as that from the temporal mass showed sympathicoblastoma (fig. 3). Because of the reaction, and the ineffectiveness of roentgenotherapy in his brother, Twin A was not given roentgenotherapy and was treated with triethylene melamine 1.0 mg. daily for three days.

The condition of Twin B, who did receive roentgenotherapy, deteriorated very rapidly. Multiple nodules appeared in the skull, a proptosis developed in the left eye and by February 28 metastases were demonstrable in all of the long bones. Twin A remained in a better nutritional state and did not develop long bones metastases until March 19, 1952 when a lesion was demonstrated in the left ulna. However, his head enlarged rapidly, with multiple nodules in the skull.

Twin B died on March 10, 1952 at the age of 8½ months, and nine days before the first long bone metastasis was demonstrated in his brother. Autopsy showed metastatic sympathicoblastoma in the calvarium, brain, abdominal lymph nodes, liver, testis and bone marrow of the vertebrae. The long bones were not examined.

Twin A was still alive at the age of 20 months. He had a huge head with palpable cranial metastases, and roentgenographic evidence of metastases in most of the long bones. The right testis was enlarged, suggesting a metastasis similar to that found at autopsy in his brother. For about the last five months he appeared to have had a remission. The various lesions had not increased in size and notwithstanding the large head he was quite vigorous. He could walk with help, could say a few words, could eat well, and weighed nearly 26 pounds. Repeat roentgenograms in February 1953 showed recession and recalcification of all the bone metastases, except one in the region of the occiput. The remission was apparently entirely spontaneous, since the child had had no treatment since the triethylene melamine was given on Jan. 1, 2, and 3, 1952.

#### DISCUSSION

It is highly improbable that either of these infants could have been saved. Although Twin A is still alive and appears to be having a spontaneous remission, his ultimate outlook is certainly hopeless. It is interesting that he should have survived so long when only one course of triethylene melamine, over a three day period, was given 13 months previously. The brother who was treated by roentgenotherapy had a rather severe reaction and succumbed to metastatic tumor very quickly. Since there are so many variables, it is obvious that no conclusion can be drawn from these facts, so far as treatment is concerned. When surgical

removal of sympathicoblastoma has been early and radical, a number of rather long survivals have been reported, both with and without postoperative roentgen-therapy. If permission for operation could have been obtained when first requested, Twin A might have had a better chance for a longer and possibly metastasis-free survival, if not for cure.

In this particular instance the tumors were of a type carrying a very poor prognosis, and they occurred in young infants. It is evident, however, that the clinical application of the principles suggested by these cases and those previously reported may well be life-saving in many situations. Snyder<sup>13</sup> in his monograph on medical genetics comments that "—there exists a brilliant opportunity for the physician to diagnose early, and thus in many cases to cure, cancer in relatives of cancer patients. In the case of an identical twin this opportunity should never be overlooked."

The recognition of a tumor in one of a pair of identical twins should make the clinician instantly alert to the possibility of a tumor in the other twin. The likelihood of concurrence may vary somewhat with the age of the twins and the type of tumor although information on this point remains inadequate. The genetic factor in cancer of the breast is quite well recognized, but the parts played by chemical and physical irritations, such as coal tar, tobacco tars, exposure to irradiation, for example, have not been completely established. It is reasonable to believe that a genetic tumor diathesis may be present in identical twins, but if one is a heavy smoker and the other does not use tobacco, the smoker may have a better chance of acquiring bronchogenic carcinoma than his nonsmoking twin. It is known, however, that bronchogenic carcinoma can occur in nonsmokers, and the general principle of alertness toward the identical twin of a known cancer patient remains sound, regardless of the type of tumor. Furthermore, the unaffected twin may develop a malignant tumor of a different type and in a different location, as in the cases cited by Macklin, referred to previously.

In general, when the cancer is discovered in one twin during infancy or early childhood, the likelihood of concurrence is probably even greater than it is in adults, since the genetic factors are more likely to predominate. Therefore, although vigilance with respect to the apparently healthy twin is strongly to be recommended at any age, it is especially important in the tumors of early life. The cases here reported represent an example of this general principle.

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## RESPIRATION AND ANESTHESIA\*

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*Baltimore, Md.*

Some three years ago, H. J. V. Morton<sup>6</sup> wrote in an article devoted to this subject: "Since the earliest days in anesthesia, respiration has provided helpful signs for those who conduct fellow human beings on journeys through unconsciousness. We have no reason to suspect that the last secret has been revealed; that no more useful information is forthcoming. Let us then apply ourselves with renewed vigor to the study of respiration, and progress in anesthesia will surely result." The literature has contained many such studies in the three years since Morton's article appeared.<sup>1, 5, 7, 8, 12, 13, 14</sup> For those whose interests lie in this direction anesthesia is a peculiarly fertile field for exploration.

Alterations in respiration provide the most reliable signs of depth of narcosis during anesthesia. Deep ether anesthesia, sodium pentothal, cyclopropane, morphine, curare and other drugs employed by the anesthetist all depress respiration and therefore necessitate constant attention to and, frequently, support of respiration. In this connection the avoidance of respiratory acidosis associated with inadequate alveolar ventilation has been the subject of numerous articles in recent years. Finally the maintenance of an open airway and the avoidance of undue resistance to breathing are problems present during every moment of every anesthesia.

In view of these facts it is remarkable that in this age of exact measurement the anesthetist is generally forced to estimate the adequacy of his patient's ventilation by observing or feeling the excursions of a rubber bag which, when full, holds 5 liters of gas. Even the most skilled and experienced person cannot hope to estimate such excursions accurately. As a result most of us have relied on our ability to err on the side of overventilation. Even a superficial perusal of recent literature suffices to demonstrate how frequently the error occurs on the other side. Automatic machines and special measuring devices have been developed<sup>2, 3, 4</sup> but none has come into general use due to expense, awkward, cumbersome or unreliable equipment, and, to some degree, to unwillingness of the anesthetist to learn new methods.

Our interest to date has been directed towards a better understanding of the problems related to respiration during anesthesia rather than towards the development of equipment of practical use to the anesthetist.

The pneumotachograph provides a convenient method for visualizing various characteristics of respiration. From it one can readily see the respiratory rate, observe certain characteristics of the movement of air both in and out of the

\* This work was supported by Grants in Aid from the U. S. Public Health Service. Presented during the Louisville Assembly of the Southeastern Surgical Congress, Louisville, Ky., March 9-12, 1953.

† From the Division of Anesthesiology, Department of Surgery, The Johns Hopkins University School of Medicine.

lungs, and approximate the volume of ventilation, both as to minute volume and tidal volume.<sup>9, 10, 11, 15</sup> The pneumotachograph is a record of the speed of air movement in and out of the lungs in relation to time. Thus in a single cycle one sees from the start of inspiration at zero velocity the changing speed of air flow into the lungs (above the zero line), and the subsequent pattern of expiratory flow velocity below the zero line. The area lying between the zero line and the velocity line represents volume of air moved.

Although the apparatus required for recording the pneumotachograph is expensive, it need not be cumbersome and can be placed where it may be readily observed by the anesthetist. The pneumotachometer itself can be placed in the

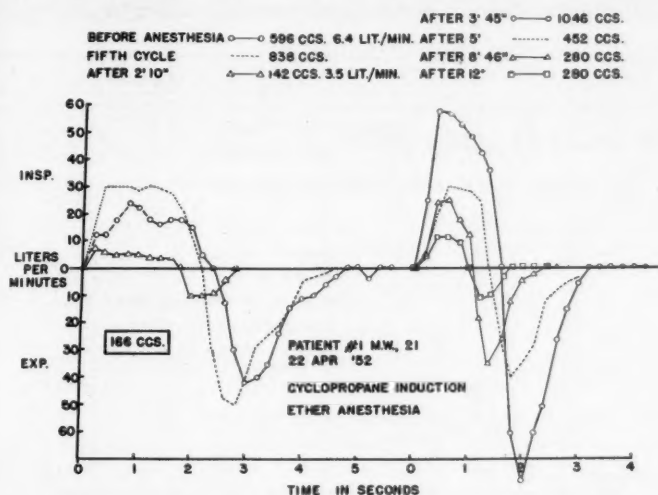


Fig. 1. Cyclopropane depression of respiration. Secondary depression with deep ether anesthesia.

airway without significantly adding to dead space or handicapping the anesthetist in his maneuvers.

The following data are presented, not because they add startling new knowledge, but because they illustrate some of the ways in which a quantitative measurement of respiration may be of use. Two normal subjects were studied in some of the various positions most commonly used during surgical operations. No significant alterations in respiration were noted in these 2 subjects. However, the positions were maintained for only a few minutes. Further exploration of the effects of position on respiration under a variety of circumstances should be done.

Patient 1, M. W. aged 21. Orthopedic procedure on lower extremity under cyclopropane-ether, in supine position. Premedicated with morphine and scopolamine. Preanesthetic minute volume was 6.4 liters, with tids of 596 cc. (fig. 1).

After 2 minutes the tids had fallen to 142 cc. with a minute volume of 3.5 liters. This was in part due to depressed respirations, but also due to breath holding and coughing (figs. 2

and 3). With the addition of ether, respirations deepened, but after 12 minutes lower third plane anesthesia had reduced tids to 122 cc. with a minute volume of 3 liters. Respirations were assisted and assisted tids of over 1 liter were obtained (fig. 4). During the procedure obstruction to the airway developed. The change in pattern is readily noted as well as the return to normal subsequent to lifting the chin (fig. 5).

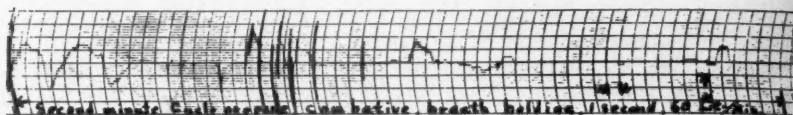


Fig. 2. Note poor ventilation during this minute largely due to breath holding and coughing. Shortly after this regular but depressed respirations commenced (see figure 1).



Fig. 3. Note pattern of good assist coming in about one-half second after initiation of inspiratory effort.

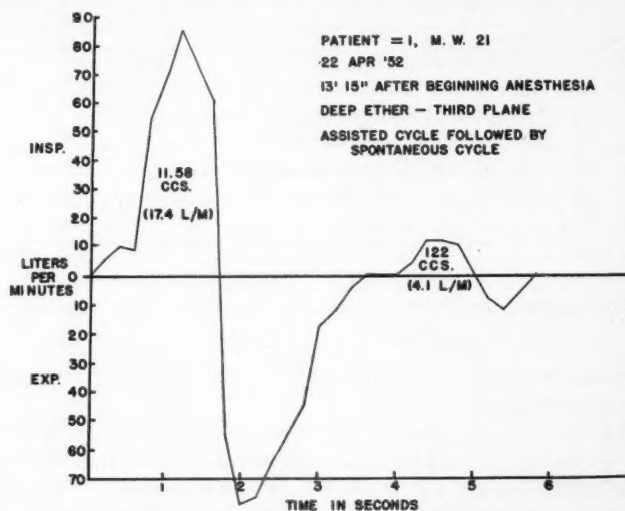


Fig. 4. Note the rectangular pattern with developing obstruction and relief on elevating chin.

Patient 2, F. W. aged 16. Mitral commissurotomy under cyclopropane ether anesthesia. Sincurine (decamethonium) used for intubation. Right lateral position. Premedicated with demerol and atropine.

Preanesthetic minute volume was 4.5 liters, with tids of 247 cc. Respirations returned about 3 minutes after sincurine had been given for intubation, but were markedly depressed (fig. 6). Controlled respiration was begun and continued through most of the procedure.

During the postsyncurine depression tids were 86 to 191 cc. with minute volumes of



2.4 to 5.7 liters. With control, tidsals of about 1 liter were possible with minute volumes of about 20 liters. The type of spontaneous respiration just before and after opening the pleura is well illustrated (fig. 7).

Patient 3, M. W. aged 29. Pyelolithotomy under spinal anesthesia. Left lateral kidney position. Premedicated with morphine and scopolamine. Preanesthetic tidsals were 860 cc. and minute volume 14.3 liters. This was undoubtedly attributable to extreme apprehension on the part of the patient. After 42 minutes in the extreme kidney position this patient still had tidsals of 477 cc. and minute volume of 8.7 liters (fig. 8).

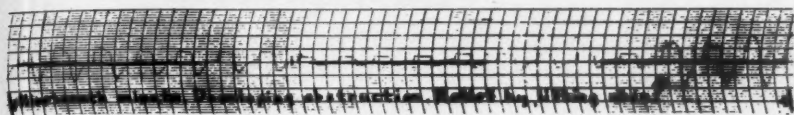


FIG. 5. Severely depressed respirations, and the beginning of assisted cycles.

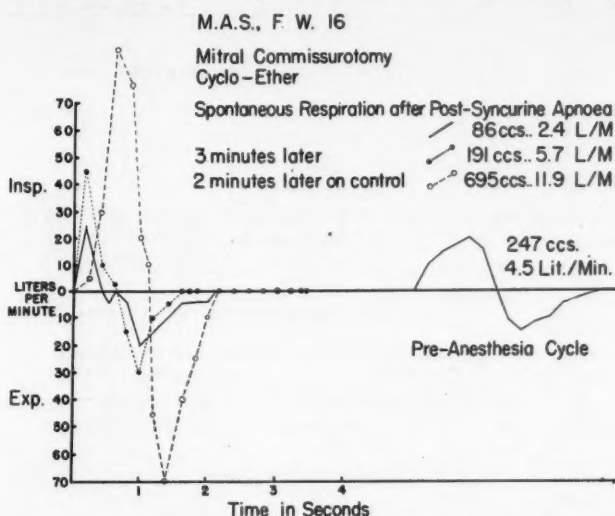


FIG. 6. Note wholly inadequate tidsals three minutes after return of spontaneous respiratory effort.

Patient 4, M. W. aged 44. Nephrectomy under spinal anesthesia and light (upper first plane) sodium pentothal, nitrous oxide, and oxygen. Supine position with slight Trendelenburg. Premedicated with demerol and scopolamine.

Preanesthetic tidsals were 1066 cc. and minute volume was 10.5 liters. This patient also was quite apprehensive. When placed in the severe kidney position after spinal anesthesia, but before supplementing with general anesthesia, tidsals dropped to 523 cc. but minute volume was maintained at 10 liters.

He was moved to the supine position and general anesthesia begun without any alteration in his respirations. Tidsals never fell below 423 cc. and minute volume ranged between 10 and 15 liters (fig. 9).

Patient 5, F. W. aged 72. Cholecystectomy under spinal anesthesia and light (upper first plane) sodium surital and nitrous oxide-oxygen. Supine position. Premedicated with demerol and scopolamine.

Preanesthetic minute volume was 7.3 liters, with tidsals of 363 cc. There was no marked alteration of respiration until the general anesthesia was begun. Tidsals then fell to 224 to 300 cc. with minute volume of 2.4 to 4 liters per minute. Periodic assistance of respiration was necessary throughout (fig. 10).

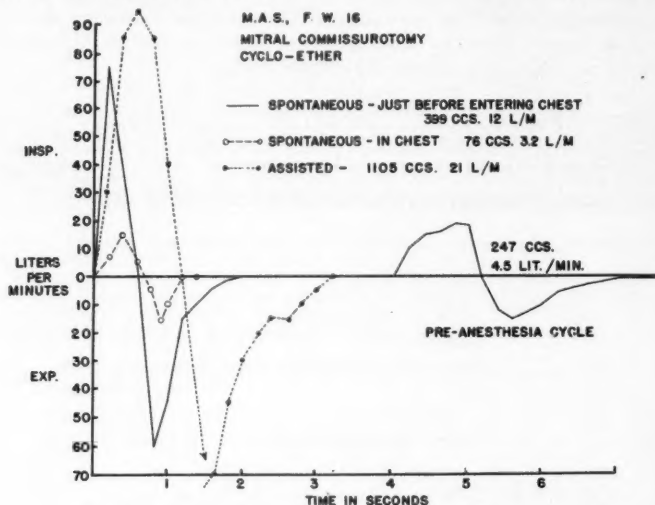


FIG. 7. Effect upon ventilation of opening pleural cavity.

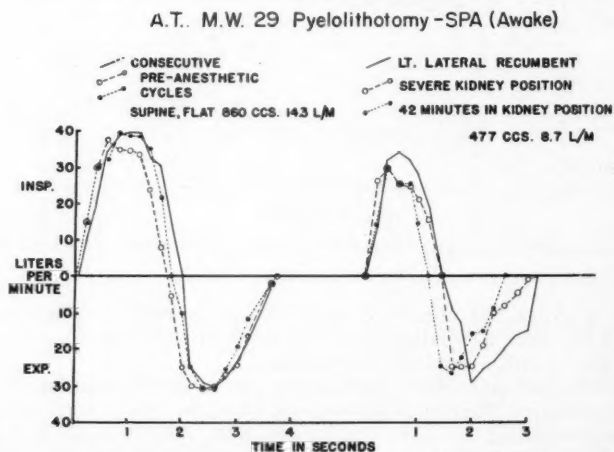


FIG. 8. Spinal anesthesia alone. No significant reduction in ventilation after 42 minutes in kidney position.

Three patients have been studied in relation to the adequacy of ventilation in the prevention of respiratory acidosis during open chest procedures. The attack on this problem has only just begun and the object of future work will

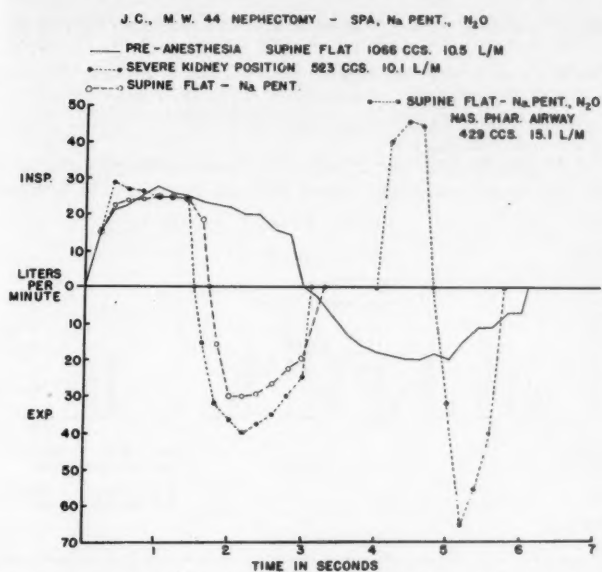


FIG. 9. This patient continued to have good tiduals and minute volumes throughout light sodium pentothal supplementation of spinal anesthesia. Severe kidney position prior to pentothal did not decrease ventilation significantly.

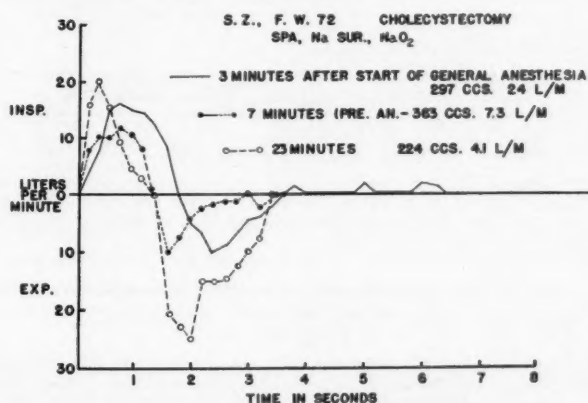


FIG. 10. All three cycles show smaller tiduals than preanesthetic (363 cc.). Note prolonged post-expiratory pause in cycle three minutes after first injection of sodium surital.

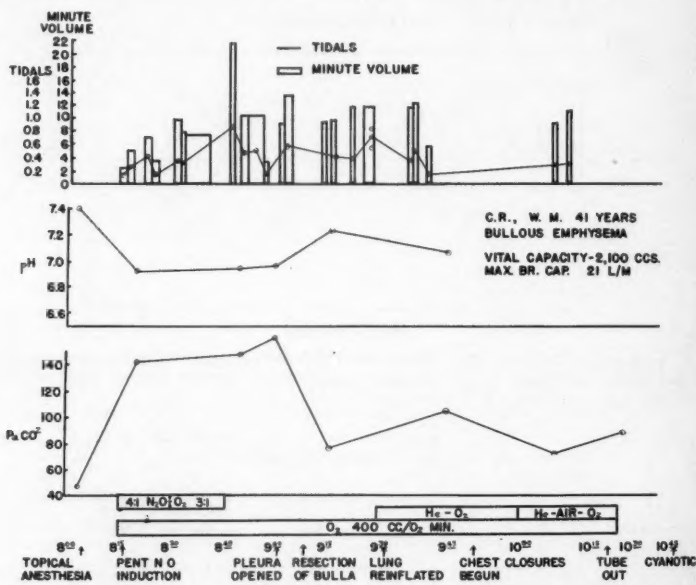
be the determination of factors influencing the ventilatory requirements of such patients.

Patient 6, M. W. aged 41. Resection of giant pulmonary bullae. Local anesthesia for intubation and sodium pentothal-nitrous oxide-oxygen. Right lateral position. Premedicated with demerol and scopolamine. This patient suffered from severe pulmonary emphysema

and his maximum breathing capacity ranged from 17 to 52 liters per minute. He was dyspneic at rest.

Although his ventilation was maintained between 7 and 21 liters per minute, after the first 15 minutes of the operation his arterial  $p\text{CO}_2$  rose to 156 at one time and was 79 at the conclusion of the procedure. The pH of his blood fell to 6.92 at one point. He survived the operation and has done well (fig. 11).

Patient 7, M. C. aged 36. Resection of pulmonary bullae. Sodium pentothal anesthesia, with syncurine for intubation. Right lateral position. Premedicated with demerol and scopolamine.



to say that, although ventilation was adequate as demonstrated by the low  $p\text{CO}_2$ , there was apparently a 15 per cent venous admixture during the operation upon this patient. That is to say that approximately 15 per cent of the blood passing through this patient's lungs was inadequately exposed to alveoli which had been properly ventilated. It was also possible to calculate that her physiologic dead space had been increased to 50 per cent of her tidal volume. Approximately 50 per cent of each tidal volume which this patient breathed during the operation was not being adequately exposed to pulmonary venous blood.

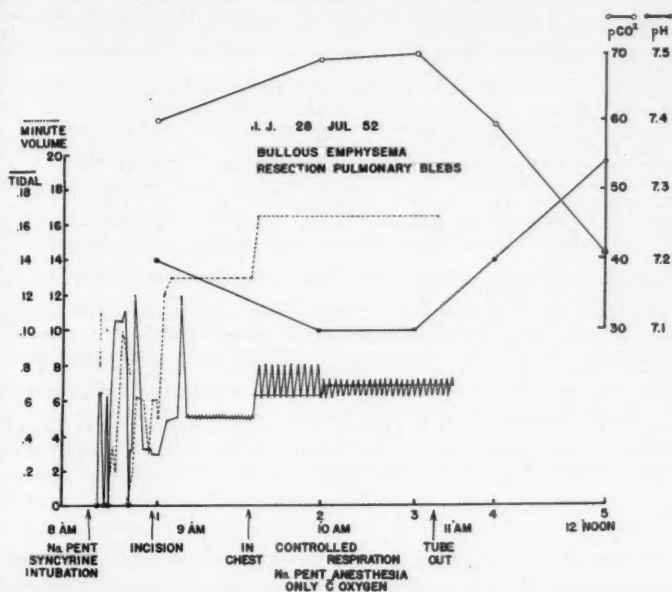


FIG. 12. Note elevated  $\text{Pa CO}_2$  and low pH while ventilation was at rate of 16 to 18 liters per minute and tidals of 600 to 800 cc. Note inadequate ventilation just after intubation.

These findings indicate that there is a disproportion between ventilation and perfusion of some alveoli during open chest operations, even in such a relatively healthy person as patient no. 8.

#### SUMMARY

These data are obviously inadequate for drawing any conclusion but do indicate that further exploration of these problems is needed.

Exact methods of measuring and studying respiration during anesthesia are needed. The pneumotachograph offers one method of observing during anesthesia and recording for exact study later, the changes in respiration which may occur.

There is some evidence of inadequate ventilation perfusion ratios during open chest procedures. Studies are under way which are aimed at further elucidation of this problem.

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## SURGERY OF PULMONARY TUBERCULOSIS\*

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The surgery of pulmonary tuberculosis presents a glorious accomplishment in the annals of surgery and in the story of man's battle against the ravages of the great white plague. It is that portion of the chapter recorded since the advent of streptomycin which will be discussed. The experience at Fitzsimons Army Hospital during the past six years based upon more than 1200 patients treated surgically will be detailed. Final evaluation of recent developments must await a five year follow-up study, however, before evidence on which to predict anticipated long term results are available.

From Jan. 1, 1947 through Dec. 31, 1952 the surgical method of choice selected in 725 patients at the Fitzsimons Army Hospital was either extrapleural thoracoplasty or extirpative measures, including lobectomy, pneumonectomy, segmental resection, or wedge excision. Follow-up data are available in 98.8 per cent of these patients. Streptomycin has been administered to 708 patients and para-aminosalicylic acid has been regularly used for the past three years. Presently, the preferable drug therapy is streptomycin, 1 or 2 Gm. every third day, depending upon the patient's weight, and 12 Gm. of paraaminosalicylic acid (PAS) daily. Isoniazid is steadily replacing (PAS). The period of drug therapy prior to operation was variable. The vast majority received therapy four to six months preoperatively and one to four months following thoracoplasty or extirpative procedures.

Extrapleural thoracoplasty was long accepted as the *sheet anchor* of the surgery of pulmonary tuberculosis.<sup>1</sup> The long term results of thoracoplasty provide a baseline for evaluating recent methods of surgical therapy. An analysis of 514 unselected patients treated by thoracoplasty at Fitzsimons Army Hospital during the period 1927 to 1946, inclusive, reveals that 47 per cent are dead. The low survival rate of that period and the present trend toward improvement is depicted in graph I. The discouraging failure in accomplishing complete rehabilitation is noted in that of the 245 surviving patients 93 per cent are receiving 80 to 100 per cent disability pension benefits.

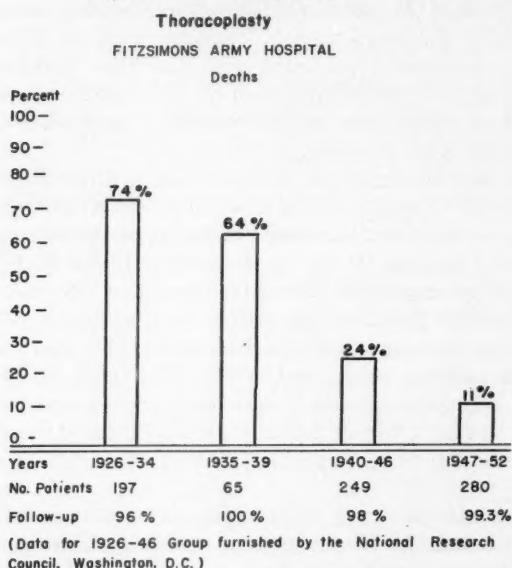
Since Jan. 1, 1947, 280 patients, including 29 who had tuberculous or mixed infection empyema, have been treated by thoracoplasty as the method of choice. The classification of the initial disease process and the number of patients in each class was: caseopneumonic, 35; fibrocaseous, 73; caseofibrous, 76; fibrous, 29; giant cavity, 38; and empyema, 29.

*Case 1.* A 33 year old white soldier became acutely ill with fever, productive cough and night sweats in November 1945. There was rapid loss of weight and sputum was positive for tubercle bacilli. The chest roentgenogram revealed extensive bilateral parenchymal

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infiltration (fig. 1). He was admitted to Fitzsimons Hospital one year later and marked clearing had occurred with bed rest and without antibiotics. Early in 1947 he was placed upon large doses of streptomycin and during May to July a three stage, seven rib thoracoplasty, left, was done without untoward event (fig. 2). He was discharged in June 1948. His disease was inactive. He has remained well and for the past three years he has been regularly employed 40 hours a week as a hospital janitor (fig. 3). He received 420 Gm. of streptomycin.

GRAPH I  
PULMONARY TUBERCULOSIS



It is our practice to do extrapleural thoracoplasty, when selected as the method of choice, usually in three operations, removing all of the first three ribs at the first stage and long segments of two or three ribs in each of the two subsequent stages at three week intervals. Occasionally a five rib thoracoplasty done in two stages provides adequate collapse of the diseased lung.

The risk entailed by a thoracoplasty in pulmonary tuberculosis is low. These 280 patients had 831 thoracoplasty operations. There were four deaths within 60 days, 3 of whom had tuberculous or mixed infection empyema. The mortality rate per operation, exclusive of empyema, was 0.13 per cent. Twenty-six have subsequently died during the six year period, a total patient mortality rate of 10.7 per cent. Eight of the 30 deaths were patients suffering from tuberculous or mixed infection empyema. Of the surviving 250 patients, 225 are one or more years postoperative. Sputum conversion from positive to negative occurred, exclusive of empyema, in 72 per cent. These data are based on 99.3 per cent follow-up information. The status of 189 surviving patients, exclusive of empyema, two or more years after operation is recorded in table I.

The removal of tuberculous lung tissue has been the principal surgical interest in this disease since the advent of streptomycin. This experience concerns ob-

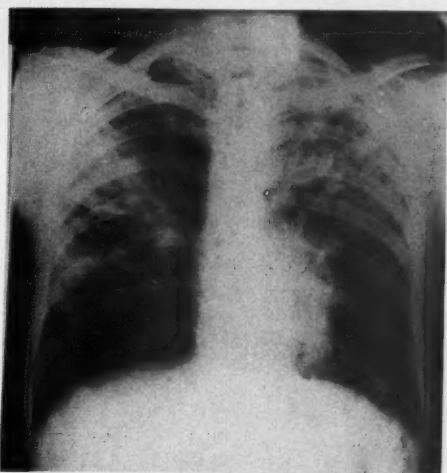


FIG. 1, Case 1. Dec. 8, 1945, acute caseo-pneumonic tuberculosis. Response to antituberculosis drugs rapid and excellent.

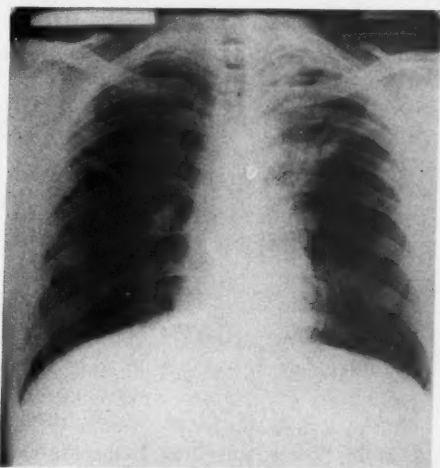


FIG. 2, Case 1. May 10, 1947, marked clearing of lesion after 11 months bed rest without streptomycin. Following large doses of streptomycin clearing continued. Roentgenogram is immediately prethoracoplasty.

servations made on 445 patients treated by extirpative surgical methods during the period Jan. 1, 1947 through Dec. 31, 1952. Our premise in the surgical attack on the local pulmonary manifestation has been predicated upon a complete con-

sideration of the patient and the protean nature of the disease.<sup>5, 11</sup> Our acceptance of the surgical removal of tuberculous lung tissue as the choice surgical therapy has been characterized by a gradual and carefully measured evaluation. In 1947 only 13 patients were treated by extirpative methods as compared to 90 treated by extrapleural thoracoplasty. Steadily the ratio has changed and is now reversed (graph II).

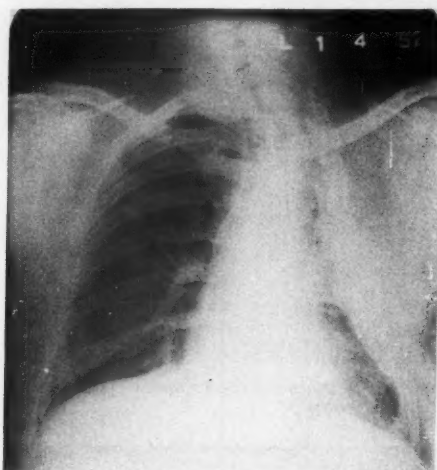


FIG. 3, Case 1. Jan. 4, 1952, three and one-half years post-thoracoplasty. He is well and has been working regularly 40 hours per week for three years.

TABLE I

*Work status*

Thoracoplasty for Pulmonary Tuberculosis\*

No. Patients	Status Two to Five Years After Operation				
	Working		Hospitalized	No follow up	Not working
	Full Time	Part time			
189	95 50.3%	37 19.5%	13 6.9%	2 1.1%	42 22.2%

\* Exclusive of empyema.

The surgical removal of tuberculous lung tissue embraces four principles. First, tuberculosis is a generalized disease usually clinically manifested in the lungs and surgical removal does not imply, in most instances, that the total area of disease is extirpated, but rather that the most involved portion is removed. This lessens repeated endogenous reinfections and aids healing by relieving the body of its chief source of tubercle bacilli. Second, the resolution of new exudative lesions is advised before extirpation. Clinical and experimental studies have

developed highly satisfactory methods for the administration of the antituberculosis drugs coinciding with the increased employment of the extirpative methods. In the presence of active disease 6 to 12 months generally elapse from the onset to surgical removal and this should include bed rest and antibiotic therapy. The application of surgery within one year is in marked contrast to prior practice. Third, the removal of one-half, or more, of a lobe of a tuberculous involved lung should preferably be preceded by one or two stages of thoracoplasty collapse of the chest wall. This lessens overdistention and probably decreases reactivation or

GRAPH II

The Increasing Use of Extirpative Surgical Methods and the Decreasing Use of Extrapleural Thoracoplasty as the Choice Method of Surgical Therapy in Pulmonary Tuberculosis.



increased activity of any disease in the remaining lung tissue.<sup>3, 10</sup> A five rib thoracoplasty and an upper lobectomy is not deforming (fig. 4). Fourth, the post-operative period of hospitalization required following extirpative surgery in the presence of remaining tuberculous lesions is variable, depending upon the extent and nature of the removed and remaining pulmonary lesions. In general, one year is recommended if lobectomy or pneumonectomy is done and six months or more for segmental resections. The application of these concepts is rapidly widening the sphere of extirpative surgery in pulmonary tuberculosis; shortening the period of hospitalization, and decreasing the dangers of reactivation. In our experience, indications for other independent surgical methods are rapidly decreasing.

In the consideration of extirpative measures the contralateral lung should be clear or under adequate therapeutic control. The indications used have been: (1) Tuberculoma, (2) Persistent cavitary disease. If the involvement is principally in one lobe or if bronchostenosis of the lobe bronchus is present, lobectomy is preferable. This includes most of the thoracoplasty failures. (3) Persistent active noncavitary disease. The resolution in response to the antituberculous drugs is often so striking that only small residual foci, demonstrable roentgenologically, remain. These residual lesions should be removed and they generally contain tubercle bacilli with uncertain potentialities as to their viability since the organisms seldom grow on culture. (4) Bronchostenosis of a main stem bronchus. Pneumonectomy is indicated. (5) Certain suspected but unconfirmed tuberculous lesions, exclusive of tuberculoma.

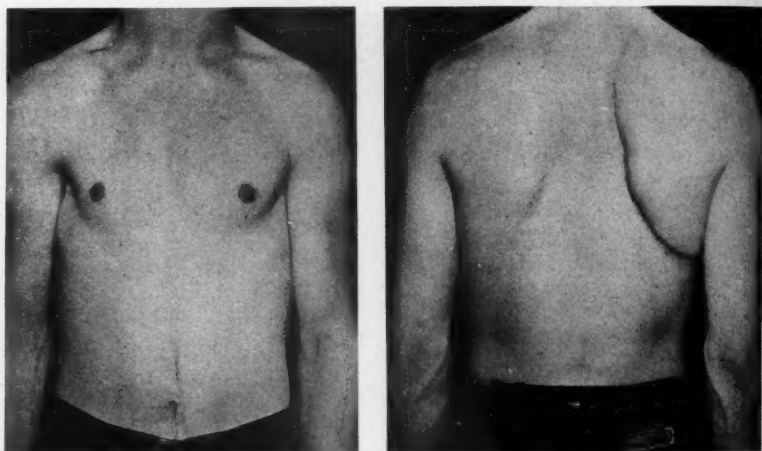


FIG. 4. Front and back view of a patient who has had a five rib thoracoplasty and right upper lobectomy in the treatment of pulmonary tuberculosis. He is well.

The pulmonary tuberculoma is the focalization of a tuberculous pneumonia by fibrous encapsulation appearing as a somewhat rounded, usually subpleural, pseudo tumor with satellite nodules.<sup>9</sup> They are unpredictable lesions; slow to calcify; difficult to distinguish from neoplasms; require experienced judgement as to their surgical management, and respond favorably to extirpation. Sixty per cent have had daughter satellites close to or some distance from the main nodule. Eighty per cent have been detected incidental to chest roentgenographic examinations in individuals without symptoms considered due to tuberculosis. In 53 per cent of the patients, the surgical specimens contained tubercle bacilli. In the remainder, pathologists long experienced in pulmonary diseases considered the etiology to be tuberculosis. Recent experiences with the identification of histoplasma capsulatum from lesions indistinguishable roentgenographically from the tuberculoma may validate the previous observations.<sup>6</sup> The tuberculoma is



classified as either *ripe* or *mature*, indicating that tubercle bacilli are not demonstrable, or as *unripe* or *immature* indicating that tubercle bacilli are demonstrable. In the progress of their development there is no satisfactory criterion upon which to base a prediction as to whether or not the process will go on to maturity. They may persist apparently unchanged for years; then cavitate; break through their fibrous barrier, and disseminate tubercle bacilli with reactivation of the disease process. In an experience with 83 patients lobectomy was used in 32, segmental resection in 5, and wedge excision in 46. Twenty-three of these patients were operated upon prior to 1947. These patients are usually good surgical risks. There were no operative deaths and only 1 has since died 30 months after operation from gradual disease progression. The surgical removal of tuberculous lung

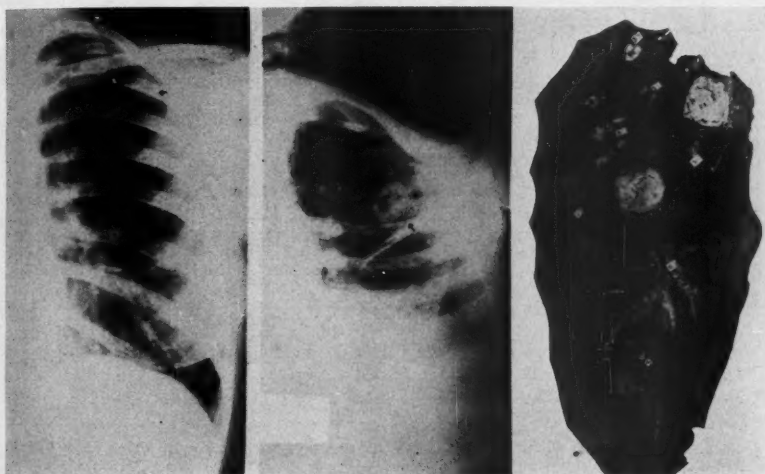


FIG. 5, Case 2. Undiagnosed lesion, right upper lobe, and surgical specimen. Tuberculoma which has cavitated. Tubercle bacilli isolated from lesion.

tissue containing the tuberculoma offers the most feasible approach to their management.

*Case 2.* A 30 year old white woman had had a 10 year history of an undiagnosed pulmonary lesion which was first noted on a routine chest roentgenogram. Therapy had been characterized by a short period of sanatorium bed rest in 1944 and 1945. In July 1947 symptoms of undue fatigue, loss of 17 pounds in weight during the past six months and cough resulted in her hospitalization at Fitzsimons Army Hospital in April 1948. Repeated efforts to isolate *M. tuberculosis* from the gastric content and sputum were repeatedly negative. Chest roentgenogram revealed moderately extensive nodular lesions in the right upper lobe. Lobectomy, right upper lobe, was done August 17, 1948. Streptomycin was given as protection. The surgical specimen revealed a fibrocaseous nodose tuberculosis with beginning cavitation in a large tuberculoma (fig. 5). A three rib upper stage thoracoplasty, right, had been done July 12, 1948. She remained in the hospital one year. She is now well, and has had no recurrences. For 10 years this patient had been suspected of having tuberculosis, but bacteriological evidence was lacking and the diagnosis was not made until the lesion,

which proved to be a tuberculoma that had broken through its fibrous wall, was removed and *M. tuberculosis* was demonstrated in the surgical specimen.

During the period of this experience cavitory disease has presented the major problem in the surgical removal of tuberculous lung tissue and lobectomy has been the most effective surgical method used. One hundred sixty-seven patients with cavitory disease were treated by lobectomy during the period from Jan. 1, 1947 through Dec. 31, 1952. One hundred thirty-six are one or more years postoperative. The sputum conversion in this latter group, defined as immediate change from positive to negative and consistently negative for one year or longer, occurred in 81.6 per cent. This is in contradistinction to sputum conversion following thoracoplasty wherein one or two positive sputums have been noted in 20 per cent of those designated as converted. An additional 5 per cent converted within 12 months after operation. A total of 14 remained positive. Eight and four-tenths per cent of the 167 patients are dead. The work capacity of 101 surviving patients, who are two or more years postoperative, is noted in table II.

TABLE II  
*Work status*  
Lobectomy for Cavitory Disease  
January 1 1947 to December 31 1950

No. Patients	Working		Not Working	No Follow-up	Hospitalized
	Full time	Part time			
101*	52 51.4%	28 27.7%	13 12.8%	3 2.9%	5 4.9%

\* Not including 11 deaths.

*Case 3.* A 25 year old white soldier had mild upper respiratory symptoms for a few days prior to a routine chest roentgenogram taken at the time of his re-enlistment Aug. 18, 1950. A cavitory area 4 by 4 cm. with considerable surrounding parenchymal infiltration was noted in the right lower lung field. The sputum was positive for *M. tuberculosis*. Streptomycin and para-aminosalicylic acid therapy given for four months resulted in considerable clearing, but the cavitory lesion persisted (fig. 6). Right lower lobectomy was done Dec. 15, 1950. The surgical specimen revealed a cavitory lesion of tuberculosis measuring 4.5 by 3.5 cm. and contained numerous *M. tuberculosis*. He is well and has been on active military duty at Fitzsimons Army Hospital working as a movie projectionist since October 1952.

As the beneficial results of the antituberculous drugs became increasingly evident the surgical extirpation of active noncavitory disease by lobectomy, segmental resection, or wedge excision has brought about increasingly favorable results. Of 83 such patients treated by lobectomy, including 6 in the tuberculoma group, 57 are one or more years postoperative. Sputum conversion in this latter group, defined as immediate change from positive to negative and continuing negative one year or more, has been high, 97.6 per cent. This striking conversion rate is a strong endorsement for the use of antituberculous drug therapy and extirpative surgery in the absence of cavitory disease.

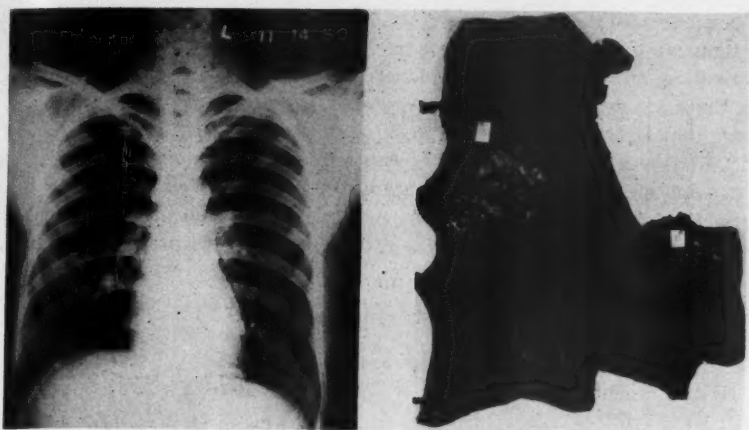


FIG. 6. Case 3. Cavitory lesion, right lower lobe. Surgical specimen, right lower lobe, demonstrating cavitory lesion.

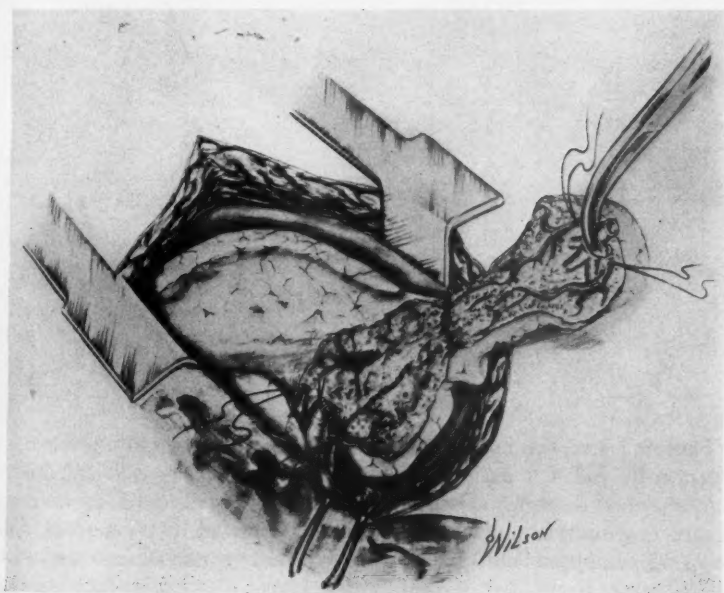


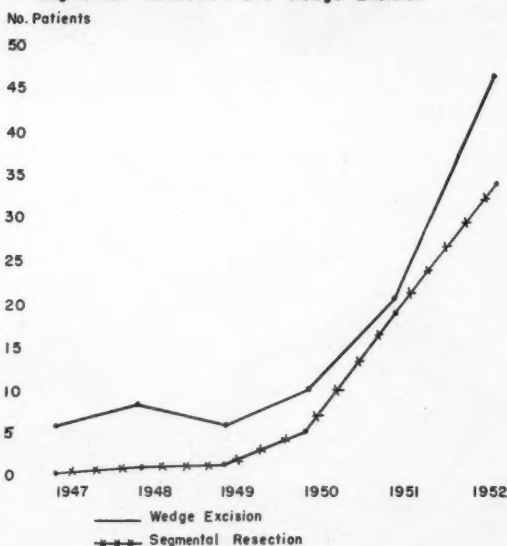
FIG. 7. Artist's drawing depicting segmental resection of left upper lobe.

The use of segmental resection of the disease process involving principally one or two bronchopulmonary segments is steadily increasing (fig. 7).<sup>2</sup> The excision of well localized residual lesions by wedge excision, exclusive of the tuberculoma, is also increasing. Actually *more and more* patients with *less and less* tuberculosis

are being treated with increasingly favorable results. This trend is good in that the removal of residual foci containing *M. tuberculosis* decreases the danger of reactivation and reduces the period of hospitalization. In efforts to conserve lung tissue a degree of hesitation is suggested. If more disease tissue is allowed to remain than is removed or if tiny lesions, not discernible by roentgenography or difficult to detect by palpation of the exposed lung are frequent causes for surgical exploration, then enthusiasm for segmental resection is excessive. The steady rise in the use of segmental resection and wedge excision of tuberculous lung tissue is interesting (graph III). This experience is too recent to permit evalua-

GRAPH III  
PULMONARY TUBERCULOSIS

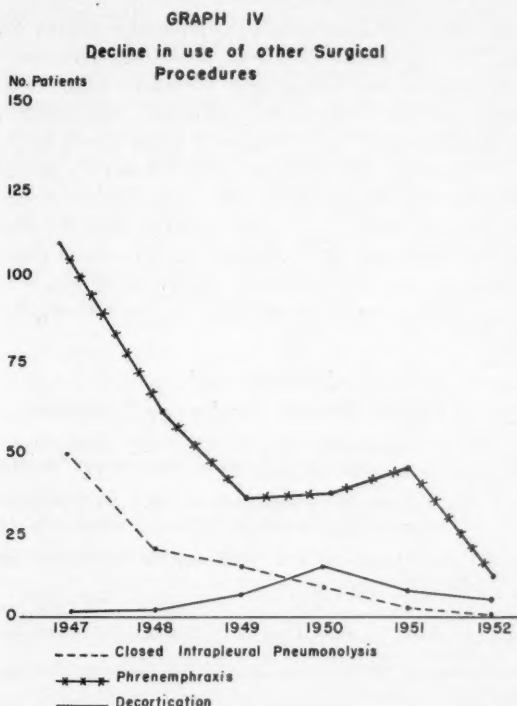
Segmental Resection and Wedge Excision



tion. Sputum conversion has occurred in each patient whose sputum was positive preoperatively and it is anticipated that more than 95 per cent of patients in whom segmental or wedge resection is properly indicated and done will be able to return to gainful employment. Two patients treated by segmental resection developed an empyema and 1 had a bronchopleural fistula. All recovered without further surgery. None of these complications developed in the patients treated by wedge excision.

Complications with these extirpative procedures have been few. Bronchopleural fistula developed in 3.0 per cent of the patients treated by lobectomy and empyema in 2.6 per cent. Spread of the disease within a six month postoperative period following lobectomy occurred in less than 2 per cent. The operative mortality rate, including all deaths in 60 days, for lobectomy in 267 patients with

pulmonary tuberculosis has been 1.5 per cent. In a consecutive series of 618 pulmonary lobectomies for all causes, the mortality rate has been 0.8 per cent. All lobectomies have been done by the individual ligation of the hilar structures.<sup>8</sup> Endotracheal gas-oxygen-ether anesthesia with sodium pentothal induction has been given by competent anesthetists. The surgery has been done expeditiously but haste in operating has been avoided. The blood loss, as determined by blood volume determinations 24 hours after operation, averaged 2495 cc. compared to the estimate of 1349 cc. made at the time of operation by the dry weighed



sponge method. Blood replaced during operation has exceeded by about 40 per cent that calculated as lost by the dry weighed sponge method.<sup>7</sup>

Pneumonectomy, in our experience, has seldom been indicated in the treatment of pulmonary tuberculosis. We agree with Churchill in that "the principles that introduce total pneumonectomy into the treatment of pulmonary tuberculosis are totally different from those that underlie lobectomy."<sup>4</sup> In 445 patients treated by the surgical extirpation of tuberculous lung tissue the procedures used have been: wedge excision, 22 per cent; segmental resection, 13 per cent; lobectomy, 60 per cent; and pneumonectomy, 5 per cent. The indications now used for pneumonectomy are bronchostenosis of a main stem bronchus or a totally de-

stroyed lung. The contralateral lung should be clear. The mortality rate and complications have been much higher in the pneumonectomized patients. Of 22 patients upon whom pneumonectomy was done, 18 per cent developed a bronchopleural fistula and empyema. Twenty-one per cent of pneumonectomized patients are dead.

The use of surgical methods other than thoracoplasty or extirpation has rapidly declined, (graph IV).

#### SUMMARY

The surgery of pulmonary tuberculosis has advanced rapidly since the advent of streptomycin. The experience at Fitzsimons Army Hospital has been presented which emphasizes the increasingly favorable effect which extirpative surgical methods, especially lobectomy, segmental, and wedge excision, have had during the past six years. Final appraisal of these efforts must await a longer interval. In this experience 423 patients were treated by extirpative surgical methods, exclusive of pneumonectomy, and the operative mortality, including all deaths within 60 days, was 1.2 per cent. Presently available data indicate that it is reasonable to predict that approximately 90 per cent of patients treated by these methods have or will be completely rehabilitated and able to engage in gainful occupations. This completely reverses the experience prior to the advent of streptomycin.

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## SURGICAL MANAGEMENT OF ADRENOCORTICAL TUMORS

### WITH REPORT OF A CASE\*

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The mortality rate following the surgical removal of functioning tumors of the adrenal cortex has declined notably in recent years. Among the factors which have contributed to this decline are the ready availability of more complete replacement therapy; a better understanding of the physiologic effects of adrenocortical hormones; an increased knowledge concerning the morphologic pathology of adrenocortical tumors; and the identification of the predominating steroids secreted by different types of these tumors. It has been pointed out that it is the tumor which is secreting an excess of corticoids, as opposed to the tumor secreting an excess of 17-ketosteroids, the removal of which is the more likely to be followed by postoperative adrenal crisis (table I).<sup>4</sup> Kenyon<sup>6</sup> has constructed a practical classification of syndromes based upon clinical findings. This has proved useful, but modifications will unquestionably be made in the future. In fact, the whole tendency to classify these tumors on the basis of the physical characteristics which they produce may be superceded by a classification based largely upon the chemical characteristics of the steroids excreted in the urine. Kenyon's clinical classification (with minor modifications) follows:

1. Adrenogenital syndrome: in children of either sex but more frequently in girls and occasionally in adult women, masculinization may be intense.

2. Cushing's syndrome: in women and children, masculinization is much less intense than in the adrenogenital syndrome and consists mostly of abnormalities in the growth of hair. There may be a *buffalo* type of obesity, a plethoric appearance with a *moonlike* face, hypertension, purple striae, ecchymoses, osteoporosis and diabetes mellitus. Amenorrhea is usually present in women. Masculinization may be associated with adrenocortical hyperplasia, adrenocortical tumors, thymic tumors with adrenal hyperplasia, ovarian arrhenoblastoma, adrenal rests of the ovary, and pituitary tumors with or without adrenal hyperplasia.

3. Mixed clinical pictures which include features of both the first two categories. For example: there may be present hypertension, striae, and glycosuria, individually or together, where intense masculinization is present.

4. A type characterized by single or isolated endocrine manifestations.

5. Feminizing syndromes, a rare manifestation in men characterized by atrophy of the testes, loss of body hair, and growth of the breasts. Girls may show precocious breast enlargement and menstruation.

6. Pseudohermaphroditism and true hermaphroditism.

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## 7. Tumors without endocrine function.

This brief clinical classification is not intended to be exhaustive. For additional information more detailed sources may be consulted. In contradistinction to most functioning tumors of the other endocrine organs, the functioning tumors of the adrenal cortex are frequently malignant. This imposes an additional responsibility upon the surgeon doing the operation, and it imposes more severe limitations upon the prognosis.

TABLE I\*  
*Urinary corticoids vs. urinary 17-ketosteroids†*  
(Modified from Engstrom)

Origin.....	Corticoids	17-ketosteroids
	Adrenal cortex	Adrenal cortex and testes
Number of carbon atoms in precursors	21	19
Examples of precursors	Compounds A, B, E, F, and desoxycorticosterone	Testosterone and adrenal androgens
Normal daily excretion‡	0.12 to 0.3 mg./24 hrs. in both sexes (Talbot)	Men, 6 to 25 mg. (avg. 14) Women, 5 to 17 mg. (avg. 10)
Metabolic action of precursors	Influence carbohydrate, protein and fluid metabolism	Promote nitrogen retention, muscular strength and weight gain
Effect of trauma on excretion	Increased	Less consistently increased

\* Certain generalizations are used.

† Hardy, J. D., *Surgery and The Endocrine System*, Philadelphia, W. B. Saunders Company, 1952, p. 6.

‡ The value obtained for the normal daily excretion of corticoids varies with the method used. The method in use in our laboratory gives a normal value of from 5 to 8 mg. per 24 hours.

The purpose of the present report is to present a case of functioning adrenocortical carcinoma together with physiologic studies which emphasize certain points of clinical, chemical, anatomic, and pathologic interest.

## CASE REPORT

History and physical examination: The patient was a slender 26 year old married white woman employed as a medical secretary. She had been well until approximately two years before admission when her menstrual periods had become irregular, with lengthening intervals between periods. Approximately one year before admission she had begun to have intermittent febrile episodes associated with general malaise, backache, pain in the right flank, and a sensation of fullness in the upper abdomen. Studies at that time had failed to explain her symptoms on the basis of an infective agent. These studies included complete blood counts, urinalyses, routine serum agglutinations for the typhoid groups and brucella, he-

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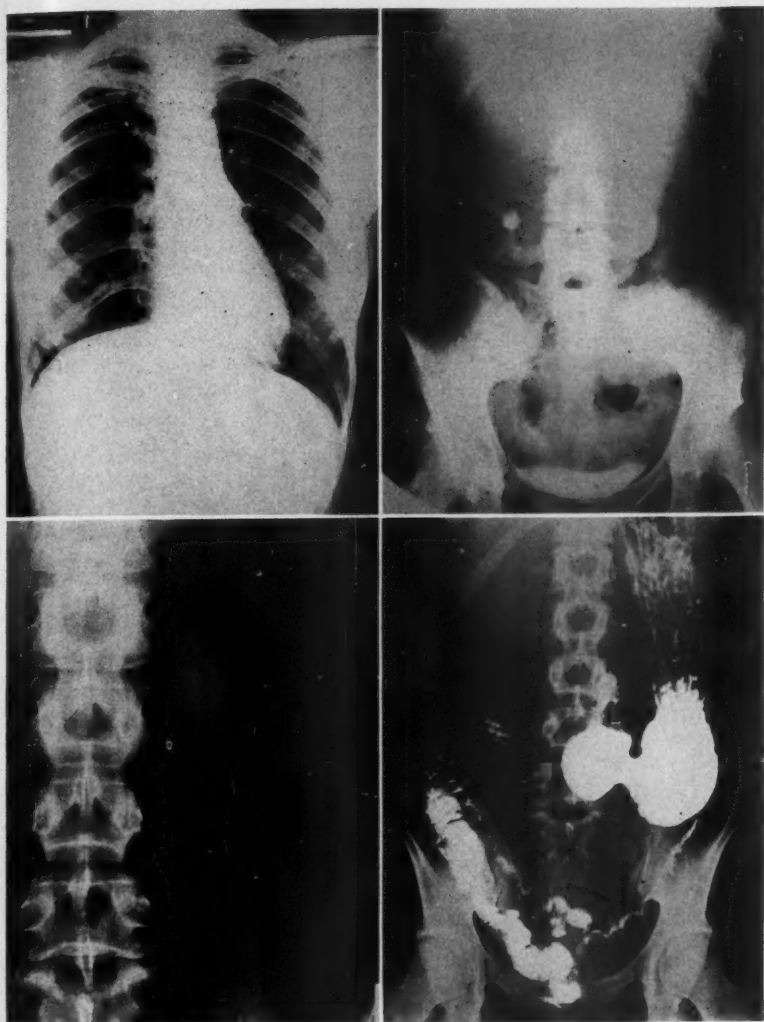


FIG. 1. Roentgenologic Studies In Right Adrenal Tumor. Upper Left: This chest roentgenogram shows mild elevation of the right diaphragm with moderate displacement of the heart to the left. Upper Right: The intravenous pyelogram shows downward displacement of the right kidney. Lower Left: The cholecystogram reveals displacement of the gallbladder into the left upper quadrant. Lower Right: The gastrointestinal series presents some downward displacement of the pylorus and duodenum and, in addition, the lateral roentgenogram presented some anterior displacement of the body of the stomach.

terophile antibody titer, gross liver function studies, and repeated chest roentgenograms which showed some elevation of right diaphragm and possible displacement of the heart to left. Shortly following these studies the febrile attacks had subsided, as had the other symptoms, with the exception that the patient did not again feel entirely well. A sense of dis-

comfort in the throat led to a tonsillectomy in August 1951. However, thereafter she continued to lack energy and upon occasion she was again aware of the sense of fullness in the epigastrium. Her periods ceased entirely in the winter of 1952. Pregnancy was suspected but was ruled out. Three weeks before admission to the hospital on May 19, 1952, she again developed fever, associated with considerable pain in the epigastrium and right flank. At that time an excretory intravenous urogram, barium enema, upper gastrointestinal barium examination and cholecystogram were done. All showed an extrinsic mass situated in the right upper quadrant with displacement of the surrounding organs (fig. 1).

At this point the patient was referred to one of us (J. D. H.) and the following additional findings were elicited. Her voice sounded slightly *throaty* to the examiner and in response to questioning the patient stated that, while she had noted no particular change in her speaking voice, she could no longer sing high notes. The suprapubic hair distribution was definitely of the male type. She stated that this distribution had developed only during the past six months, during which time she had also noted an increase in the hair around her nipples and on her upper lip. Neither of the last two findings was particularly prominent. Her breasts were small and flat. An abdominal mass situated chiefly in the right upper quadrant moved downward on deep inspiration, descending almost to the umbilicus; it was firm and not tender either to palpation or to fist percussion. Although the mass seemed

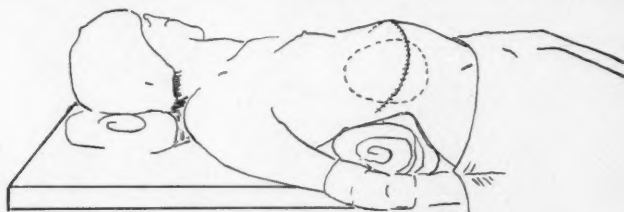


FIG. 2. Subcostal Incision For Adrenal Tumor. This incision is a reasonably satisfactory one for the removal of large tumors. One disadvantage of this exposure, however, is that it may prove difficult to divide adhesions between the tumor capsule and the diaphragm under direct vision, and troublesome bleeding may result. When it appears desirable, therefore, the subcostal incision should be converted into a thoracoabdominal incision (fig. 8).

to be adherent to the liver, an indentation was felt between the two which led the examiner to suspect that the main portion of the mass was not liver. The mass was irregular and seemed to be lobulated. There was no auscultatory bruit.

The pelvic examination revealed the probable identity of the mass. The clitoris was prominently in evidence and was enlarged to a length of approximately 2.5 cm. A clinical diagnosis of a masculinizing tumor of the right adrenal cortex was made.

The laboratory findings substantiated the clinical diagnosis. The 24 hour urinary excretion of total neutral 17-ketosteroids was 280 mg. (average normal value for females 10 mg.) and the excretion of corticoids was 30 mg. (average normal for laboratory 5-8 mg.).\* Thus, while the urinary excretion of both groups of steroids was elevated, the excretion of 17-ketosteroids was enormously and preponderantly increased, resulting in almost purely masculinizing features (adrenogenital syndrome) without such Cushing syndrome features as apparent obesity, hypertension, striae, and glycosuria. The fasting blood sugar level was 85 mg. per 100 ml. The serum carbon dioxide combining power was 43 volumes per cent (19 mEq./L.) and the serum chloride level was normal. Preoperative serum sodium and potassium analyses were lost through a technical mishap. The fasting total eosinophil count was 58 cells per cu. mm., and this value was considered to be low. The non-protein nitrogen level was normal.

\* The detailed steroid excretion studies in this patient will be the subject of a separate report.

**Preoperative management:** Two days before the planned operation, ACTH was begun intramuscularly on a dosage schedule of 25 mg. every six hours. The purpose of this therapy was to utilize the secretory capacity of the large adrenal tumor to increase the concentration of adrenal steroids in the tissues; further to diminish the likelihood that adrenal crisis would occur postoperatively. That this therapy was effective in increasing the secretory activity of the tumor was evidenced by a prompt and marked increase in the urinary excretion of 17-ketosteroids. However, the excretion of the more highly valued corticoids did

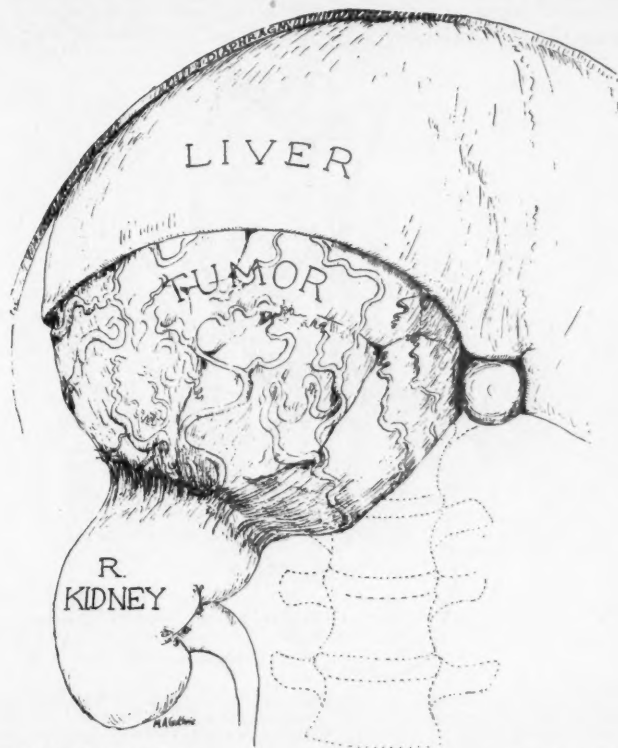


FIG. 3. Right Adrenocortical Carcinoma. The tumor was encapsulated, and it was possible to identify planes of cleavage which permitted separation of the mass from the surrounding organs. Numerous vascular adhesions to the diaphragm gave rise to troublesome bleeding, and the denuded undersurface of the right lobe of the liver had to be packed to achieve hemostasis.

not increase. Commercial supplies of cortisone, desoxycorticosterone acetate, and adrenocortical extract were made readily available.

**Operation:** On May 26, under endotracheal anesthesia, the abdomen was explored through a right subcostal incision as indicated in figure 2, and an encapsulated volley-ball size right adrenal tumor was exposed. The surface of the tumor was traversed by many large veins, and it was found to be firmly adherent to the under surface of the right lobe of the liver, the right leaf of the diaphragm, the vena cava, and the upper pole of the right kidney (fig. 3). The incision was extended both medially and laterally, and attention was first directed to separating the tumor from the right kidney. This proved to be relatively



simple once the extensive vascular connections had been divided and the proper cleavage plane identified (fig. 4). It was believed that the branch of the renal artery to the adrenal had been divided and ligated with the many other connecting vessels, but this was not the case. As the large tumor was delivered into the wound this vessel was avulsed from the renal artery, and the defect in the renal artery was closed with no. 00000 Deknatel silk. The tumor was thereafter successively freed from the diaphragm, liver, and the vena cava. The vena cava was densely adherent to the tumor over a distance of almost 8 cm., and not until it had been separated from the tumor by alternate blunt and sharp dissection was it possible to visualize, ligate, and divide the large adrenal vein and the superior and middle adrenal arteries (fig. 5). A perforation in the tumor capsule the diameter of a finger tip was



FIG. 4. Separation of Adrenal Tumor From Renal Capsule. This dissection was not difficult. The right inferior adrenal artery, which arises from the renal artery, should be carefully identified and ligated before an attempt is made to fully deliver the tumor into the wound (see fig. 5).

produced at the point where the adrenal vein emerged from the mass to enter the vena cava. Otherwise the encapsulated tumor was removed intact.

The size of the tumor, together with the extensive and extremely vascular adhesions, resulted in much venous bleeding along the under surface of the liver and the right leaf of the diaphragm which, in large part, had to be controlled with moist gauze packs until the tumor could be delivered and better exposure secured. There were brief intervals of hypotension upon the operating table, but these responded readily to the rapid infusion of blood. Even after all actively bleeding points had been ligated it was found impossible to control with sutures the continuous ooze from the large denuded undersurface of the right lobe of the liver. Accordingly, the liver bed was packed with gauze rolls, the ends of which were brought out through a stab wound. The main wound was then closed with continuous chromic no. 0 catgut in the peritoneum, interrupted no. 30 stainless steel wire in the fascial layers, and interrupted cotton sutures in the skin.

Postoperative management: At the close of the operation, which lasted two hours, the



condition of the patient was judged to be satisfactory. She had received 50 mg. of cortisone intramuscularly at the time the adrenal vein was divided and she was placed on a post-operative dose of 50 mg. intramuscularly every six hours. A slow but continuous intravenous drip of 5 per cent glucose in 0.85 per cent saline solution was maintained. A dose of 5.0 mg. desoxycorticosterone acetate was begun, to be repeated every 24 hours. Penicillin was administered prophylactically. Cortical extract was not given but was held in ready reserve. A close watch was maintained for a rise in temperature, an unduly rapid pulse, or a fall in blood pressure, should the appearance of any of these signify impending adrenal crisis. The urinary output was closely checked, and morphine for pain was used sparingly.

Seven hours postoperatively her rectal temperature had risen to 103 F. Cold sponging was begun to control the fever, but notwithstanding this the temperature rose two hours

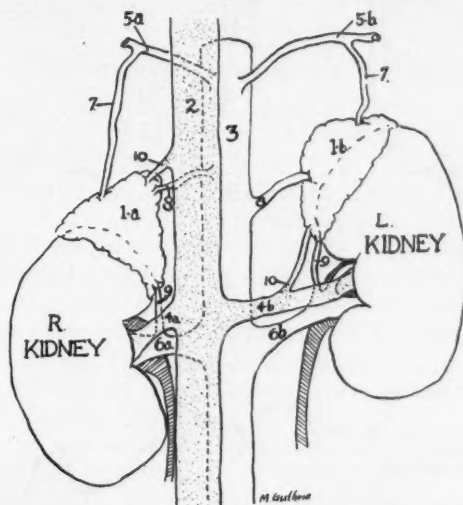


FIG. 5. Adrenal Vasculature. 1a. Right Adrenal. 1b. Left Adrenal. 2. Inferior vena cava. 3. Aorta. 4a. Right renal vein. 4b. Left renal vein. 5a. Right phrenic artery. 5b. Left phrenic artery. 6a. Right renal artery. 6b. Left renal artery. 7. Superior adrenal artery. 8. Middle adrenal artery. 9. Inferior adrenal artery. 10. Adrenal vein.

later to 104.2 F., where it was to hover for almost 36 hours. However, since she had no hypotension and her urinary output was good, no adrenal cortical extract was given at that time. Forty-two hours following operation she experienced a definite, if ill defined, crisis which was manifested physically by apprehension, restlessness, dyspnea (40 per minute), tachycardia (130 per minute), nausea, and mild disorientation, and we had great difficulty in maintaining the rectal temperature below 104 F. even with continuous sponging with a cold alcohol-water mixture. The lungs were clear to auscultation. The blood pressure was 142/70. The precise etiology of these symptoms was uncertain. As it was possible that the replacement therapy might have resulted in an overloading of the circulation, particularly in view of the fact that the blood pressure had actually risen, only 10 cc. of cortical extract was administered. Aspiration of the stomach netted only 10 cc. of bile stained fluid. Intramuscular prostigmine for moderate abdominal distension resulted in the passage of a considerable amount of flatus. Whatever therapy was most effective, the symptoms of nausea and dyspnea began to subside, and the next morning, almost exactly 48 hours after operation, a rather sudden profuse sweating was followed promptly by a fall in rectal temperature from 104 F. to 101 F. (fig. 6). Thereafter her convalescence was steady and uneventful.

The ACTH therapy, having been discontinued at the time of operation, was resumed on

## PHYSIOLOGICAL CHART

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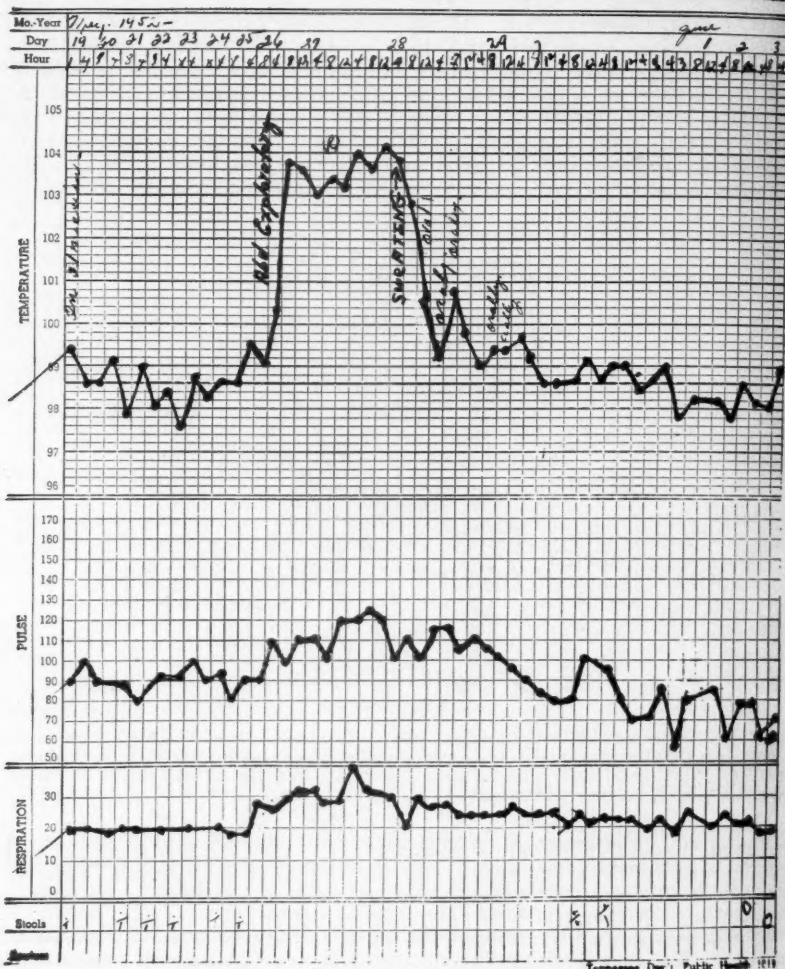


FIG. 6. Clinical Chart Before and Following Resection of Functioning Adrenocortical Tumor. Several hours following operation there was a sharp rise in body temperature which persisted for about 48 hours. Such fever is common following the resection of a major portion of the functioning adrenocortical tissue. The physiologic mechanism of the fever, other than that it results from an insufficiency of cortical function, is obscure (see text).

the second postoperative day to stimulate the opposite (remaining) adrenal gland, which was considered likely to have become somewhat atrophic in the presence of such an actively functioning tumor on the contralateral side. Too, while the patient's own pituitary gland could be depended upon to secrete some ACTH, in the presence of the fairly large daily cortisone dose (200 mg.) it seemed possible that the activity of the patient's pituitary gland would have been partially suppressed. This concept of pituitary suppression by endo-

crine therapy was fairly well supported by a temporary diminution in the urinary steroid excretion after the postoperative ACTH therapy was withdrawn on the tenth postoperative day. The desoxycorticosterone was discontinued on the third postoperative day. The dose of cortisone was reduced to 150 mg. on the third postoperative day; to 100 mg. on the fifth postoperative day; to 50 mg. on the sixth postoperative day; to 25 mg. on the seventh postoperative day, and was discontinued altogether on the eighth postoperative day. The packing had been easily withdrawn in stages, and the patient was allowed to travel to her home 400 miles distant on the sixteenth postoperative day. The patient regained her health and menses, and remained well until four months later, when she returned for re-examination. Unfortunately, at that time her urinary steroids were found to have again increased and a few days later hepatic metastases became prominent, resulting in death.

#### DISCUSSION

##### *Gross and Microscopic Pathology of the Tumor (R. S. J.)*

The tumor measured 15 by 17 cm., and its capsular external surface was found to be interrupted at the site of emergence of the adrenal vein, as mentioned in the description of the operation. On the cut surface there was seen a very soft pale grayish-pink tissue somewhat duskier than flesh color. There was a tendency for the tumor to be divided by thin septa into 2 to 4 cm. lobulations which bulged above the general plane of sectioning. A uniform, fine texture without whorl or plane formation was present. There were no cysts within the tumor, but there was a 4 by 5 cm. area of yellow necrosis centrally in the mass (fig. 7).

Microscopically, the characteristic and uniform cell type was of moderate size, with a granular type nuclear and chromatin material without very distinct cell borders. The cytoplasm was about equal to the nucleus in size. A few nucleoli and a few mitoses were seen. In occasional areas larger cells were seen, and these cells often had large hyperchromatic granular nuclei. Rarely, a multinucleated cell was seen. The cells were arranged in broad patternless masses, although a slight suggestion of cord-like formation was to be seen due to the encircling of the thin walled vessels by the cells.

A portion of the capsule was examined and neoplastic tissue was noted prominently within the vessels and sinusoids throughout its wall. Most of the capsule seemed to be composed of irregularly laminated collagen. In the outer portion considerable hyalinized material was noted and some distorted neoplastic cells appeared there as well. The tumor cells seen within the vessels were, of course, considered to be of unfavorable prognostic significance.

A small portion of the tumor was analyzed by a semiquantitative method for 17-ketosteroid content, and it was found to contain excessive amounts of these steroids.

The final diagnosis was that of carcinoma of the adrenal cortex with marked blood vessel invasion.

##### *The Fever which follows Adrenalectomy in Man*

It has been our experience that the operative removal of a large part of the functioning adrenocortical tissue in man is likely to be followed by a sharp rise in body temperature, although this is at variance with at least some reports concerning adrenalectomy in animals. The mechanism of this fever is not clear. Since it would appear that body temperature may be raised by an increase in

heat production, by a decrease in heat loss, or by a combination of both, the question arises as to which of these possibilities should be held responsible for the fever following adrenalectomy in man. In the light of animal experimentation, it is not obligatory to assume that there is a marked increase in heat production.<sup>11</sup> Nevertheless, the balance which appears normally to exist between thyroid activity and adrenocortical activity has surely been altered. To clarify



FIG. 7. Excised Adrenocortical Carcinoma. The tumor measured 15 by 17 cm. and the cut surface was grayish-pink in color with the exception of a 4 by 5 cm. yellowish area of central necrosis. There was widespread blood vessel invasion. The 17-ketosteroid content of the tissue was analyzed by a semi-quantitative method, and it was found to be very great.

this point, it may be noted that thyroid crisis has been treated successfully with large doses of cortical extract,<sup>7, 8</sup> and that the administration of ACTH and cortisone have been shown to lower the serum level of thyroxine and related compounds.<sup>9</sup> Therefore, when the adrenal tissue is removed in a normal man the normal thyroid activity is abruptly *unopposed* and perhaps may be, in effect, at a toxic level. Conceivably the *unopposed* normal thyroid activity could produce the early postoperative febrile response which frequently follows adrenalectomy in man. It will be recalled that the resection of a toxic thyroid gland frequently results in a febrile response which is maximal during the second 24

hour period and then usually subsides thereafter. Similarly adrenal crisis, if it is to ensue following resection of an adrenal tumor, usually intervenes during the first 48 hours. The patient herein reported had her maximal rise in fever during the first 48 hours. However, attractive as is the thyroid-adrenal balance hypothesis, it has marked limitations. Rather, we are inclined to place more emphasis on the possibility of a decrease in heat loss, to account for the fever following adrenalectomy. It has been found that following major surgical operations the patients tend to sweat less readily into a rubber glove,<sup>3</sup> and the fall in temperature which occurred in our patient at the end of 48 hours was preceded by profuse sweating. Furthermore, the patient who has had an adrenalectomy may have

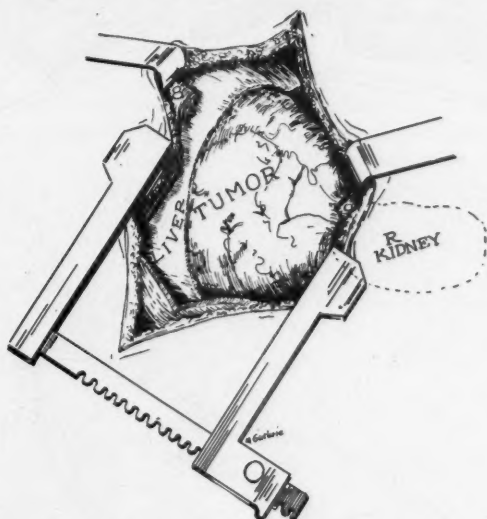


FIG. 8. Thoraco-abdominal Incision For Adrenal Tumor. A transverse or subcostal incision in the upper abdomen may be readily extended into the chest through the eight or the ninth interspace. The advantage of such an exposure over that of the simple subcostal or the kidney incision is that, in the case of large tumors with extensive adhesions, bleeding points along the diaphragm and the undersurface of the liver can be controlled under direct vision.

still other factors which tend to increase body temperature. For example: in impending adrenal crisis the blood volume and the extracellular fluid volume are diminished. This would diminish the circulation to the body surfaces and the normal cooling (heat loss) would not occur. The fluid dynamics by which the diminished extracellular volume is produced in adrenal failure have been studied by Gaudino and Levitt.<sup>2</sup> The administration of desoxycorticosterone results in a movement of water from the intracellular to the extracellular fluid compartment, augmenting the plasma volume. Presumably this improvement in the efficiency of the circulatory system would result in a more efficient cooling of the body.

Clearly, the factors which may influence body temperature following adrenalectomy are complex.



*Operative Exposure of Adrenal Tumors*

Although we experienced no great difficulty in resecting this large tumor through a long right subcostal incision (fig. 2), we believe that the loss of blood could have been substantially reduced had there been better exposure of the diaphragmatic and hepatic adhesions. The patient had been intubated preoperatively in order that the subcostal incision could be safely converted into a thoraco-

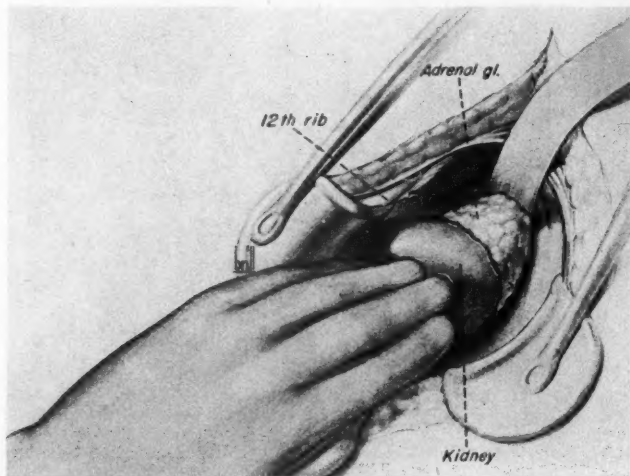
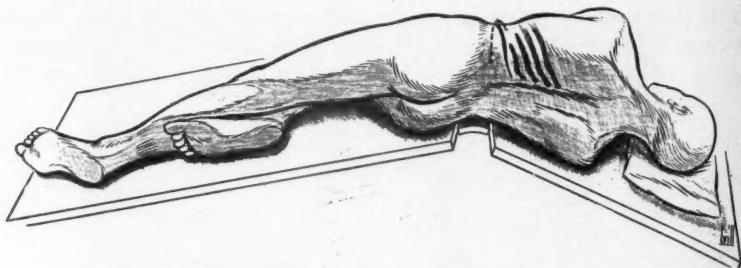


FIG. 9. Loin or "Kidney" Incision For Adrenal Tumor. Above: Usually the twelfth rib need not be resected. Below: The renal capsule had been omitted for clarity. Exposure of the adrenal is frequently more readily accomplished if the renal capsule is not opened. Hardy, J. D., *Surgery and The Endocrine System*, Philadelphia, W. B. Saunders Company, 1952, p. 124-125.

abdominal exposure, should the situation require it, but the difficulty in securing exposure was never quite sufficient, in our opinion, to justify the extension of the incision into the thorax. However, we shall in the future employ the thoraco-abdominal incision for the excision of such large adrenal tumors (fig. 8). A purely thoracic incision might make the abdominal dissection difficult. Berman and Mainella<sup>1</sup> found it impossible to remove a 9 by 8.5 by 6 cm. right adrenocortical tumor through the loin incision (fig. 9) in a 3 year old girl, and Walters<sup>10</sup> has noted the rather serious bleeding which may result from the vascular attachments



to the diaphragm. Nevertheless, the loin or kidney incision is quite satisfactory for the resection of small tumors or of normal adrenal tissue.

#### *Endocrine Therapy*

Walters and Sprague<sup>10</sup> have well expressed the dictum that every adrenocortical tumor should be treated as if adrenal crisis was expected to follow its removal. Thorn<sup>9</sup> has suggested the use of ACTH preoperatively, to use the great secretory capacity of the tumor to flood the patient's tissues with an excess of adrenal steroids. This suggestion was used in our case with fair results. Because of the expense of adrenocortical extract, we believe that cortisone in large doses, supplemented with DOCA and saline-glucose solution infusions may safely be used first. However, adrenocortical extract should be on hand and, if the other therapy proves inadequate, the extract should be used in whatever doses are necessary to hold in abeyance the symptoms and signs of adrenal crisis. In particular, it is most important that significant hypotension be prevented, but care must be exercised to avoid too much therapy. The one point which is most to be emphasized is that these patients must be followed constantly by a competent observer during the critical first three days.

#### SUMMARY AND CONCLUSIONS

General types of physical syndromes which may be produced by functioning adrenocortical tumors have been described.

The preoperative, operative, and postoperative management of a functioning adrenocortical tumor has been discussed.

The advantages and disadvantages of different surgical approaches to the adrenal glands have been considered.

The mechanism of the fever which follows adrenalectomy in man remains in question.

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## CERTAIN PRACTICAL CONSIDERATIONS IN THE MANAGEMENT OF CARCINOMA OF THE LUNG\*

BASED ON AN ANALYSIS OF TWO HUNDRED AND THIRTY-  
FIVE FATALITIES

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In carcinoma of the lung, even more than in most other varieties of malignant disease, a tragic irony exists. We have perfected our surgical technics, and there is no doubt of their potentials, yet the best results that the most experienced thoracic surgeons can accomplish is a 5 per cent five year salvage. Two-thirds to three-fourths of all patients are inoperable when they are first seen. From one-third to one-half of those who are explored have disease that is too far advanced to permit resection, and well over one-half of the resections that are done are merely palliative. If anything, these estimates err on the favorable side.

It is sometimes the fault of the patients themselves that their disease has passed the resectable stage when they are first seen. The cause is sometimes the nature of carcinoma of the lung, which masquerades as another disease, or which remains latent and symptomless until the condition is almost terminal. It is sometimes the inadequacy of our diagnostic methods, which, it must be admitted, have not kept pace with our therapeutic technics. Finally, in a regrettably large number of cases, it is the fault of the physician, who fails to utilize available methods; who does not use them to the best advantage, or who lacks the courage, when a precise diagnosis is not possible, to open the chest without delay and to determine, by the surest of all methods, whether the patient does or does not have carcinoma of the lung.

There is nothing at all cheerful about this disease at the present time. In the light of our present knowledge, there is not much, if anything, that we can do about a great many of its aspects. There are, however, a number of ways in which we can improve our present diagnostic performance. We would do well, I suggest, to concentrate on them, for until we improve them, we have no right at all to be complacent about our potential surgical accomplishments.

*Analysis of Cases.* Last year I reported on carcinoma of the lung in Charity Hospital of Louisiana at New Orleans for the five year period ending in 1951,<sup>2</sup> with special reference to the 186 fatalities which occurred during that time. The background of my present remarks is the same data carried through the year 1952, and with special reference to the 235 fatalities which occurred from 1947 through 1952.

During this six year period, 942 patients with carcinoma of the lung were admitted to this hospital. Of these, 347, a little more than a third, were explored.

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Of these, 147, considerably less than half, were submitted to resection, which was far more often palliative than curative. Of those submitted to resection, only 109 left the hospital alive. The mortality rate of pneumonectomy has shown some improvement as the years have passed (fig. 1). The proportion of explorations and resections has shown little improvement or none at all.

I cannot accept the reasoning, although I can understand why the argument is advanced, that it is unfair to study carcinoma of the lung from a series of

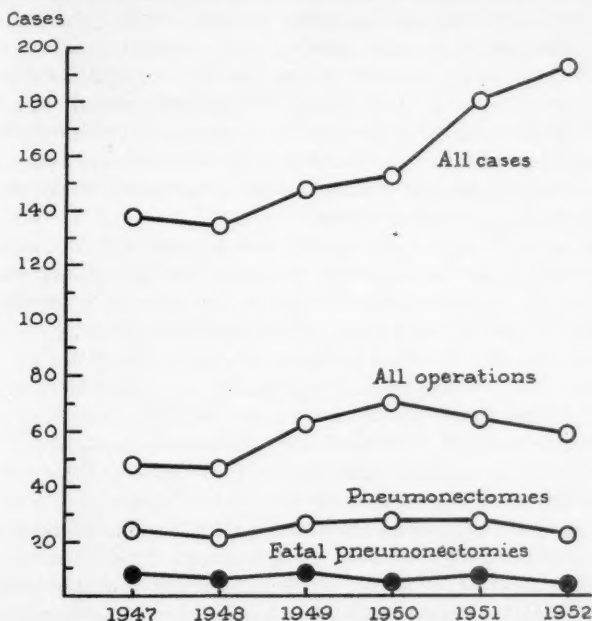


FIG. 1. Yearly distribution of admissions and operations in 942 cases of carcinoma of the lung at Charity Hospital of Louisiana at New Orleans 1947 to 1952. The 1952 figures, because all autopsy studies have not been completed, may later be altered upward.

deaths. In a disease in which, ultimately, only 5 per cent of all patients survive for five years, it would be hard to think of a more instructive source from which to study it.

*Present Incidence.* The most practical of all ways to improve results in carcinoma of the lung is to realize that it has become an extremely frequent type of malignancy. In men, in fact, it is well on the way to becoming the most frequent type. In 1912 Adler<sup>1</sup> was able to collect, from international sources, only 374 recorded cases. Today reports of hundreds of cases seen by individual surgeons are common. The situation at the New Orleans Charity Hospital is typical. Between 1910 and 1927 no record of this disease appears in the hospital files. Twenty-one cases were recorded between 1928 and June 1934. The first exploration for pulmonary malignancy was done in the hospital in 1934, and the first

pneumonectomy was done two years later. Since then, there has been a steady increase in the incidence of the disease (fig. 1). The increase, it should be emphasized, is entirely out of proportion to the increase in the hospital population.

Whether this increase is real or apparent has been hotly debated. I am in agreement with Rigler and his associates<sup>8</sup> in their contention that the master pathologists of the last century, who were at least as astute as their twentieth century successors, could not possibly have overlooked a malignant disease of such frequency. I propose, therefore, that we cease to debate the nature of the increase, and accept it as such. I further propose, in the light of the present incidence of carcinoma of the lung, that we cease to examine with an open mind patients, particularly men, over 40 years of age who complain of symptoms related to the respiratory tract. Instead, let us begin every such investigation with the strong suspicion that the patient before us may have carcinoma of the lung, and let us hold firmly to that suspicion until the diagnosis has been established, or disproved incontrovertibly, or there is sufficient evidence, in the absence of a precise diagnosis, to justify exploration.

We should go even further. We should bear in mind that any patient in the cancer age who is under investigation and treatment for another disease, even if the diagnosis is beyond doubt, may also be suffering from carcinoma of the lung. A large number of the patients who died in the Charity Hospital from this disease in the past six years had been treated in the clinics and wards for weeks, months and even years for innumerable other ailments; some trivial, some serious. Some of them were actually under treatment while their pulmonary malignancy developed and progressed, sometimes to the terminal stage. A cardinal principle in the diagnosis of carcinoma of the lung is, as these data indicate: never forget the possibility of its presence.

*Relief of Symptoms.* A second method by which we can improve our results in carcinoma of the lung is to stay our therapeutic hand when the patient is first seen. I am referring, of course, to the unfortunately general practice of attempting to relieve symptoms such as cough, hoarseness, asthmatic manifestations, and the common cold without first finding out what is the matter with the patient. It is fair to say that a major cause of the present mortality rate in carcinoma of the lung is the relief of its symptoms by the use of antibiotics and, to a lesser extent, the sulfonamides. The Charity Hospital figures prove how correct Jones<sup>7</sup> was when he said that *patients treated in this manner, especially if they went from one physician to another, were exposed to a great deal of therapy but to very little diagnostic acumen.*

Eighty-four of the 235 patients who died in the hospital over the six year period in question consulted a physician, and sometimes several physicians in succession, at longer or shorter intervals after they first experienced their symptoms. Thirteen were referred directly to Charity Hospital, in several instances with the diagnosis already made. The other 71 were treated for periods ranging from two weeks to two years with cough medicine, vitamins, penicillin, and in a few instances by all the other available antibiotics, sometimes supplemented by one or another of the sulfa drugs. Nor does all of the fault in this regard rest

with private physicians. Twenty-eight of the patients who were treated outside of the hospital were subjected to additional delay in the hospital, diagnosis and therapy, when it was possible, being delayed from 2 weeks to 12 months. In 60 patients who applied directly to the hospital, the diagnosis was delayed from two weeks to two years, and was missed entirely in 23 cases. Some of these errors were diagnostic. A very large number of them, including a number made in the hospital, arose from the practice of treating symptoms without inquiring into their causes; the practice of accepting cardiac and other diseases (which often were really present) as the explanation of respiratory symptoms; and, finally, the vicious practice of *observing* or *watching* the patient if the diagnosis could not be established promptly and without too much trouble.

Some of these patients, as has just been intimated, actually had cardiac disease and other nonrespiratory diseases. A few actually had tuberculosis in addition to carcinoma of the lung. It is difficult to understand, however, why 9 patients were treated for weeks and months for tuberculosis, with no apparent suspicion that pulmonary malignancy might be present, although acid-fast bacilli were never found in the sputum.

Elsewhere<sup>2</sup> I have called attention to the extremely dangerous tendency noted in some fatalities in this series, although not, I am glad to say, in a single instance in 1952, of invoking psychosomatic medicine to explain symptoms without first exhausting organic causes. I am not including in this charge the cases in which cerebral or central nervous system manifestations were the first indications of pulmonary malignancy. It is just as easy to see why neuropsychiatric or neurosurgical consultation was obtained in them as it is to see that patients who present this clinical picture are doomed from the outset. I doubt that the delay caused by neuropsychiatric consultation, even when it was completely unjustified, played any part in the mortality rate of these cases; all the patients died too promptly to warrant such an assumption. I think it important to emphasize, however, that another practical way to improve results in carcinoma of the lung is to resist the temptation to resort to psychosomatic causes to explain clinical symptoms whose etiology is not immediately apparent. This is a practice which seems to have charms for residents, internes and medical students as well as for practising physicians.

*Clinical Picture.* What has just been said leads to another practical consideration: carcinoma of the lung would be diagnosed more promptly if it were constantly borne in mind that it is a disease which masquerades as many other diseases and in which the typical picture frequently does not appear at all. In the 227 cases in this series in which any sort of history could be secured (some patients died too promptly for any information at all to be obtained), the history was typical in 76 and more or less suggestive in 98 others. It is hard to understand, at least in retrospect, why the diagnosis should have been missed in so many of these patients. In the remaining 53 cases, however, 23 per cent of the total number, the story was entirely atypical. Sometimes the symptoms were not even related to the chest. In some instances, such as those in which central nervous system manifestations were the first evidence of disease, the patients were



obviously doomed. In other instances, the clinical symptoms were vague because the disease was early, and the opportunity to treat it was lost because diagnosis was delayed until typical symptoms appeared. That the disease is often advanced, even in apparently early cases, is true, but this is still the most hopeful group of cases; and only a constant and very high index of suspicion will ever identify them.

Analysis of these fatalities suggests that the best possible use is not always made of such symptoms and signs as patients with carcinoma of the lung present. Physical findings are notoriously slight in early cases, but those which are elicited should be interpreted and evaluated with care. Wheezing, for instance, may be caused by asthma, but wheezing which is more prominent in one side of the chest than in the other indicates bronchial obstruction, and an immediate investigation should be undertaken to determine the cause.

The cigarette cough is extremely misleading. It may have lasted for years and the patient may have become so habituated to it that it requires persistent questioning to learn whether there has been any change in its frequency and character. One useful question is whether it is more annoying in the morning, as the chronic cigarette cough is likely to be, or is worse during the night, as the cough caused by carcinoma of the lung is likely to be.

Decided possibilities of improvement lie in the follow-up of patients in the cancer age who have had pneumonia. Recurrent pneumonia is particularly suspicious. In 27 of these 235 fatalities pneumonia developed at some time in the course of the illness, and often was the first sign. One patient had had three attacks in a year, and another five attacks in 18 months. Most of these patients were—quite properly—treated with penicillin. All of them responded well to it, and some of them responded dramatically. Even when pneumonia is superimposed on carcinoma of the lung, it can be controlled by appropriate antibiotic therapy. It is a wise precaution, however, to carry out follow-up roentgenographic studies on all patients who have had pneumonia, to be certain that there is nothing else in the chest. In one of these fatalities a suspicious density was noted in the roentgenogram while the patient was under hospital treatment for pneumonia. He recovered promptly, and a wise interne warned him to return for additional follow-up studies. This he failed to do, and there are no hospital facilities to track down such delinquents. When he did return, many months later, his condition was terminal. In another similar case the patient left the hospital against advice, and left again when the diagnosis of pulmonary malignancy was made positively on his second admission, three months later.

In six instances lung abscess was the first manifestation, or the most prominent manifestation, of pulmonary malignancy. In 1 of these cases the diagnosis was made when tissue for biopsy was taken in the course of drainage of the abscess. In 2 other cases the abscess was unroofed without this precaution and the diagnosis was not made until autopsy. These were preventable diagnostic errors, and the fact that the disease was far advanced in every instance does not make the mistake any less serious. Carcinoma of the lung is probably the most frequent



cause of lung abscess today, and pulmonary suppuration should be regarded as caused by it, unless and until another indubitable explanation can be found for it.

*Diagnostic Methods.* We are probably becoming more successful in our diagnosis of late carcinoma of the lung, but we are certainly becoming no more expert in the diagnosis of early cases. At the New Orleans Charity Hospital (fig. 1) there has been little change in the proportion of explorations and resections during the period covered by this analysis. Goldenberg and Lemon,<sup>6</sup> who studied the diagnostic results in various malignant diseases treated in a teaching metropolitan general hospital, found no improvement in carcinoma of the lung. Between 1944 and 1946 the percentage of early cases (using the very liberal definition that symptoms had lasted less than six months) was 56 per cent; between 1947 and 1950 it was 54 per cent.

Much of this failure must be laid at the door of the patient, but the physician for reasons already listed, carries an even heavier responsibility. Every reported series shows, as does the Charity Hospital series, that when the period of delay in diagnosis and therapy is divided between patient and physician, the patient's delay is usually somewhat less than the physician's. The physician, as already pointed out, tends to treat the patient for his symptoms. He is slow in using all of the diagnostic aids available to him, nor does he use them aggressively. He accepts as conclusive negative roentgenographic, bronchoscopic and cytologic reports. He lets patients slip away from observation because his warnings are not stern enough. Sometimes, as in 2 cases in this series, he advises nonsurgical therapy without giving the patient the benefit of exploration. One of these patients had a palliative pneumonectomy a year later, and the chances are that curative resection might have been possible had he been operated upon promptly, instead of being given 35 deep roentgen ray treatments. Burnett and his associates<sup>3</sup> recently reported the case history of a man who was alive and well, except for a chronic nonproductive cough, seven years after roentgenotherapy. But it should be noted, (1) that this is an extraordinary record, not likely to be duplicated very often, and (2) that before roentgenotherapy was used, exploration had proved the tumor to be nonresectable.

*Bronchoscopy.* The proportion of successful bronchoscopic examinations in these 235 fatalities (fig. 2), (74 of 130) is considerably higher than in most other series, probably because of the advanced stage of most of the carcinomas. In early cases the tumor is usually located too far distally to be seen, and biopsy section is either impractical or unsatisfactory.

I doubt that we are making the fullest possible use of bronchoscopy in the diagnosis of carcinoma of the lung. It is extremely useful in the collection of secretions for cytologic examination, the source being, of course, the most direct from which they can be secured. Furthermore, even when a positive diagnosis cannot be made, because the tumor is not visualized and tissue is not available for biopsy, there is often useful indirect evidence, which seems to have been disregarded in some cases in this series. Stenosis, hyperemia, deformity, rigidity, infiltration,

and exudation in the absence of infection are proof that some abnormal state is present. This indirect evidence, added to other evidence, may confirm the diagnosis or strengthen the decision to explore the chest.

There is little reason to do bronchoscopy in advanced cases of carcinoma of the lung, in which resection is obviously impossible. It is an ordeal, in fact, to which patients in their terminal illness should not be subjected. Four in the series died so promptly after bronchoscopy had been done that the cause and effect relationship was inescapable. Bronchoscopy is likely to be positive in such cases, but the positive report carries only academic satisfaction with it.

#### 211 X-ray Examinations:

- 150—Carcinoma positive or probable.
- 22—Carcinoma possible.
- 28—Atelectasis, effusion, abnormal density, etc.
- 11—Negative.

#### 130 Bronchoscopic Examinations:

- 74—Carcinoma (usually by biopsy).
- 56—Unsatisfactory, inconclusive, negative.

#### 105 Cytologic Examinations:

(Bronchial secretions, sputum, pleural fluid)

- 36—Carcinoma.
- 7—Suggestive.
- 62—Unsatisfactory, inconclusive, negative.

FIG. 2. Diagnostic results in 235 completely studied fatalities from carcinoma of the lung.

**Cytologic Examinations.** In the hands of experts, the results of cytologic investigation are excellent. Clerf and Herbut,<sup>4</sup> for instance, who use only bronchial washings, made a positive diagnosis by this means in something over 88 per cent of 540 consecutive cases of carcinoma of the lung. Farber and his associates<sup>5</sup> regard examination of the sputum as equally useful. If cytologic study is to be of value, however, it must be made early in the disease. Actually, as Goldenberg and Lemon<sup>6</sup> pointed out, it is seldom used until the patient is hospitalized, and hospitalized patients, for the most part, present advanced disease.

Cytologic examination (fig. 2) was positive in only 36 of the 105 cases in this series in which it was used and was suggestive in only 7 others. This is not a routine laboratory procedure. It requires a patient, as well as an experienced observer to interpret the findings. More important, from the standpoint of the clinician, it requires a special technic of fixation which, while not difficult, must be precise. It is always depressing, in a review of records such as this, to see the number of specimens reported as unsatisfactory, and to realize the wasted effort which they represent. This is one reason why cytologic examination, as it is frequently used, is a delaying method. A single positive report is all the evidence that one needs, but it is seldom secured on the first examination. The temptation therefore is great to continue to carry out serial examinations, in the hope that the next specimen will be positive. Some patients in this series had as many as 10 to 12 unsatisfactory or negative cytologic examinations, which covered as

long a period of time as 24 days. These examinations should be done daily, and my own belief is that if four or five are reported as negative, the patient's best interests are served by prompt resort to exploratory thoracotomy.

**Roentgenogram.** In this series (fig. 2), probably because the disease was far advanced, roentgenograms of the chest were diagnostic of carcinoma of the lung in 150 of the 211 cases in which they were taken, and were strongly suspicious in 22 others.

Most authorities take the position that roentgenographic examination is not useful in the diagnosis of early cases of pulmonary malignant disease. Rigler and his associates,<sup>8</sup> however, have just demonstrated that it is misinterpretation of the roentgenograms, rather than lack of roentgenographic evidence, which is responsible for this point of view. By incredible labor, they managed to locate 50 roentgenograms, in 264 proved cases of the disease, which were taken when no suspicion of carcinoma existed and when three-fourths of the patients were completely asymptomatic. When these films were reexamined, it was found that 48 per cent showed abnormal enlargement of the hilar shadow on the affected side; 38 per cent peripheral nodules; 6 per cent lung abscesses; 6 per cent obstructive emphysema, and the remainder some accentuation of the vascular trunks. These roentgenograms had been taken in industrial or other mass surveys. There was no doubt that the 50 patients had carcinoma of the lung. Thirty-four were already dead, 3 were dying, and the other 13 had been operated upon. Viewed in retrospect, all were found to have some evidence of malignant disease of the lung on or before the date it first became manifest clinically. The significant abnormalities in the roentgenograms had simply been overlooked or misinterpreted.

How important it is to investigate any roentgenographic abnormality is pointed out by Umiker and Storey,<sup>9</sup> who have just reported the first case of bronchogenic carcinoma in situ to be treated by resection after a correct pre-operative diagnosis had been made. The roentgenographic evidence of disease was a small, well defined, nodular density seen on roentgenograms taken three and one-half months after an attack of supposed acute bronchitis, which had been followed by a cough and an episode of hemoptysis. There was little delay in this case. Bronchoscopy was done, and biopsy showed epidermoid carcinoma. The cytologic diagnosis lay between carcinoma and atypical squamous cell metaplasia. Exploration revealed a perfectly circumscribed tumor, without metastases, so that lobectomy was possible. Tissue examination in the laboratory confirmed the diagnosis. As the authors emphasize, *if the investigation and prompt biopsy of relatively insignificant lesions observed on roentgenograms taken for any reason became the rule rather than the exception, many more such cases could be put on record.*

Opinions differ concerning the effectiveness of mass surveys with microfilms, such as are used for case finding in tuberculosis, in the identification of carcinoma of the lung. They have revealed a certain percentage of malignant tumors, though by no means all of the carcinomas thus identified have been incipient or early. Be this as it may, the control of carcinoma of the lung, in the light of our present knowledge, seems to lie in serial roentgenograms, preferably full size; preferably

taken at least twice yearly, in all men over 40 years of age. How practical such a plan is I am not prepared to say. I rather doubt its realism. I do believe, however, that it might be possible, as Rigler and his associates point out, to pick up far more early cases than we are now finding if there were more careful study of routine roentgenograms taken in industrial surveys and for other purposes. It would also be a fairly simple matter to question all men in the cancer age, no matter why they seek medical advice, about possible symptoms referable to the chest, and to refer for roentgenographic investigation all of those whose clinical histories are suspicious.

*Duration of Illness.* The widespread extensions and metastases in this series of fatalities (figs. 3 and 4) are probably even more widespread than the figures

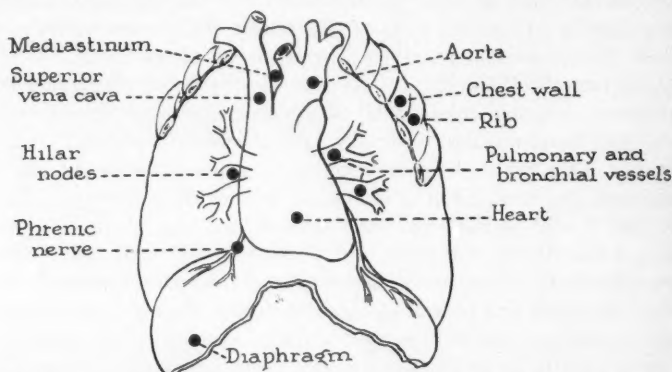


FIG. 3. Extensions and metastases within the thorax in 42 surgical and 90 autopsied cases of carcinoma of the lung. Because the 1952 autopsy studies are still not complete, the spread of the disease is probably somewhat wider than this schematic showing indicates.

indicate. For one thing: the diagrams are chiefly based on the 42 surgical cases and the 90 other autopsied cases in which the spread could be visualized. For another: exploration was seldom extensive, the state of affairs usually being obvious as soon as the chest was opened. Finally, autopsy was not always complete. Only exceptionally was permission given to open the head, and in an occasional case examination of the heart was not permitted.

In view of the extent of the disease, the brief duration of life in so many of these fatal cases is startling (fig. 5). Many of the histories bear out the known fact that *the shorter the duration of symptoms, the shorter also is the duration of life*. The most probable explanation is that in such cases *the malignant tumor is of the undifferentiated, anaplastic, fast-growing type*, which is almost never suitable for resection.

Many of these patients died shortly after they first sought medical care. In 18 of the 235 fatalities death occurred in from 5 minutes to 24 hours after they had entered the hospital. In 23 cases it occurred within 7 days. In 47 cases it occurred within 4 weeks. By the end of 2 months, 116 of the 235 patients had died.

Although these facts sound very hopeless indeed, the recent studies by Rigler

and his associates<sup>3</sup> throw a somewhat more encouraging light upon the problem. In 37 cases of carcinoma of the lung in which the natural course of the illness was not interrupted by surgery, re-examination of roentgenograms taken earlier, for one reason or another, showed roentgenographic evidence of the disease, which preceded the first symptoms by an average of seven and eight-tenths months. In

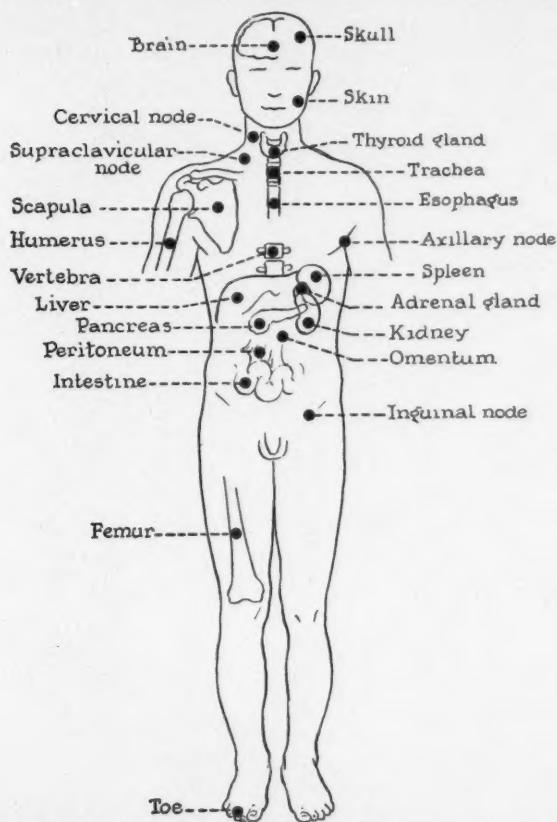


FIG. 4. Metastases beyond the thorax in 42 surgical and 90 autopsied cases of carcinoma of the lung. Because the 1952 autopsy studies are still not complete, the spread of the disease is probably somewhat wider than this schematic showing indicates.

13 cases treated surgically the discrepancy was 17 months. Actually, the discrepancy was probably somewhat greater in both groups than the figures indicate. The first films were made fortuitously, and roentgenographic signs may well have been present for much longer periods of time. As these observers interpret the findings, a new 10 month period of life has been offered to all concerned to increase the salvage of patients with carcinoma of the lung. Based upon roentgenographic signs, they estimate that the average duration of life in the nonsurgical group, in which the disease took its natural course, was 20.9 months. In the



surgical group, it was estimated to be 36.4 months. This is a longer average duration of life, Rigler and his associates point out, than any previous estimate made on the basis of symptoms alone.

*Principles of Early Diagnosis.* If we are to make use of the extra months of life which Rigler and his associates<sup>8</sup> have shown to exist in carcinoma of the lung, there must be, as these observers note, increased alertness, boldness and skill to search for tiny roentgenographic lesions on roentgenograms taken for other purposes, to suspect their nature, and to explore the chest with the idea of resecting them without, at the same time, bringing thoracic surgery into disrepute by over diagnosis and over treatment.

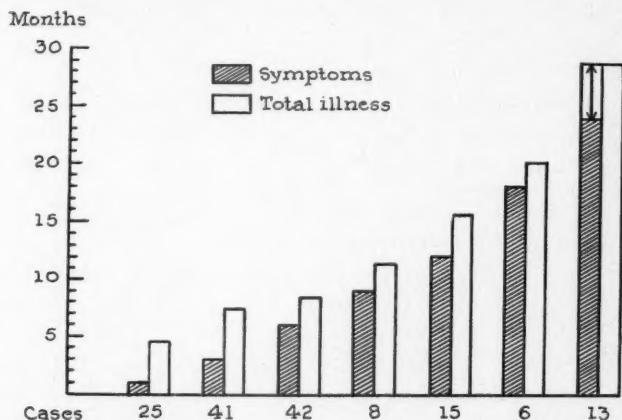


FIG. 5. Average duration of symptoms and of total illness in 150 nonsurgical cases of carcinoma of the lung.

My own very strong belief is that this is a risk which we must take. We need a great deal more courage than we are now displaying in carcinoma of the lung, both in its diagnosis and its treatment.

Let me summarize the present situation: bronchoscopy and cytologic studies are least effective in the early cases, which are most suitable for surgery. Roentgenographic examination has its limitations, but, as the investigations of Rigler and his associates show, *it is far more effective than we have previously considered it to be.* If the use of a single method establishes the diagnosis, I can see no point to proceeding with others. If the diagnosis is not established by one method, others, of course, must be used, but as far as possible they should be used, if not simultaneously, at least one immediately after the other. There is no point to the endless repetition of tests to make the diagnosis incontrovertible. There is no shadow of an excuse for watching or observing the patient.

Our objective, I think, should be to complete the diagnostic study within two weeks at the outset. If the matter cannot be positively settled within that period of time, then exploration should be resorted to. Our best hope is to be aggressive in the presence of an abnormal finding, particularly an abnormal shadow on the



roentgenogram, even if there is nothing else to point to possible carcinoma of the lung. This is a lethal disease, and the risk of exploration in the absence of a positive diagnosis is far less than the risk of delay and inaction. The period of operability is brief, and it is better to take the chance of performing an unnecessary thoracotomy than to secure an incontrovertible diagnosis in a doomed patient.

#### CONCLUSION

The conclusion of the whole matter is that *prompt exploration, even if the only justification is the physician's intuition, is our chief hope at present in the identification of early cases of carcinoma of the lung.* This point of view is neither reckless nor radical. Our past policies have been hopeless failures. What the future holds we cannot say. It is the present with which we must concern ourselves, and as of the present, exploration is the solution of the problem. It must be used far more widely and far more promptly. There will be many disappointments, for the cases which seem to be early often prove to be inoperable, but it is also true that the cases in which the diagnosis cannot be made positively are usually those which offer the best chance of cure.

#### SUMMARY

Previous methods of dealing with carcinoma of the lung have proved failures. We possess the technics and potentials for curing it, but until our diagnostic methods improve, we are unlikely to better the present 5 per cent five year salvage.

We are not, however, making the fullest possible use of such diagnostic methods as we now possess. Methods of improvement in this respect are outlined, with particular emphasis on roentgenograms taken fortuitously and for other reasons.

Our chief reliance at the present time in the diagnosis of the early, resectable case is the prompt and bold resort to exploratory thoracotomy, on justifiable evidence if it exists, on simple clinical suspicion if it does not. Both internists and surgeons must display a greater boldness than they have displayed in the past if lives are to be saved in carcinoma of the lung.

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## APPENDICITIS, ANTIBIOTICS, AND SURGICAL DRAINAGE

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Despite the beliefs of most patients and some physicians, the use of the antibiotic drugs has not satisfactorily solved all of the problems of acute appendicitis and its complications. That the use of these agents has materially aided in reducing the mortality rate in this disease is strongly suggested by a reduction in the reported over-all mortality rate of from 1.5 per cent in the preantibiotic era to the present mortality rate of less than 1.0 per cent (see table I). Although, as can be observed from table II, earlier diagnosis permitting appendectomy prior to perforation in an increasing number of cases has been a factor in our improved mortality rates, it is evident that the reduction in mortality rate has been particularly striking in cases of appendicitis with perforation (see table II). In these cases, the antibiotic agents have evidently been responsible for a reduction in the mortality rate of from 9.0 per cent reported by Keyes<sup>7</sup> in 1934 to 5.46 per cent in our experience. However, it is our belief that frequently our appreciation of the general efficacy of these agents has been too enthusiastic and has allowed wishful thinking to replace mature clinical judgment and sound surgical principles, particularly in the treatment of acute appendicitis. With this in mind, we have recently reviewed our cases of acute appendicitis to determine the extent to which the unappreciated limitations of the antibiotic agents may possibly have influenced our surgical therapy to the detriment of the patient.

*Source of Material.* Our cases are drawn from a 385 bed general hospital during the years 1947 to 1953. During this period, there were 1,984 patients upon whom appendectomy was done for acute appendicitis. The diagnosis was verified in all cases by pathologic examination of the surgical specimen or at postmortem examination. In all reported cases therapeutic doses of antibiotic agents were used, usually as an auxiliary agent. In the abscess cases it was temporarily used as the definitive form of therapy. Penicillin was administered in all cases either alone or more frequently in combination with streptomycin. Less frequently aureomycin was utilized in conjunction with penicillin, and appeared, in our hands, as in the hands of others<sup>2</sup>, to be of outstanding value, although the number of these cases was considered to be too small to be of statistical value.

*Analysis of Material.* Of our 1,984 cases of acute appendicitis, 1,816, or 91.5 per cent, were unperforated at the time of operation; 132, or 6.7 per cent, were gangrenous and had perforated to produce a diffuse peritonitis; and in 36 cases, or 1.8 per cent, perforation has occurred earlier, resulting in localized peritonitis with abscess formation (see table III). Our mortality rate in acute appendicitis was found to be 0.75 per cent. This figure is comparable to the .94 per cent reported by Schullinger<sup>14</sup> in 1950 and to 0.8 per cent recorded by Hawk and asso-

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ciates<sup>5</sup> in 1950, and tends to further substantiate the favorable influences of the antibiotics in this disease.

A further breakdown of cases on a pathologic basis is necessary to show more clearly possible inadequacies in our present management of acute appendicitis. Since it appears that the antibiotic agents are of value in all stages of appendicitis and its complications, and since adequate dose levels are usually used by all, it is only in the realm of surgical intervention that disagreement will arise as to the proper procedure to be used in a given case. The surgery to be done in such a case will, of necessity, depend upon the general condition of the patient in part, but

TABLE I

*The over-all mortality rate of acute appendicitis 1901 to 1953*

Years	Hospital	No. Cases	Mortality
1901 to 1904	Augustana Hospital, Chicago <sup>8</sup>	460	4.1%
1929 to 1937	St. Lukes Hospital, N. Y. <sup>13</sup>	793	3.2
1939 to 1945	St. Lukes Hospital, Chicago <sup>18</sup>	878	1.48
1944 to 1948	Presbyterian Hospital, N. Y. <sup>14</sup>	1,265	0.94
1947 to 1948	Henry Ford Hospital (McGraw A.B.)	1,411	.64
1947 to 1952	St. Francis Hospital, Evanston	1,984	.75

TABLE II

*The incidence and surgical mortality rate of appendicitis with perforation 1904 to 1953*

Year	Institution	Total Cases	Mortality
1904 to 1939	Frankfort Hospital, Pa. <sup>11</sup>	356	23.6%
1925 to 1939	Genesee Hospital, N. Y. C. <sup>12</sup>	145	18.0
1944 to 1945	Cook County Hospital, Chicago <sup>10</sup>	136	13.0
1939 to 1945	St. Lukes, Chicago <sup>18</sup>	153	5.8
1947 to 1952	St. Francis, Evanston	128	5.46

usually to a much greater extent upon the type of the pathology present. It is, therefore, valuable to assay our results in the treatment of appendicitis and its complications in relation to the pathologic picture encountered.

*Acute Appendicitis without Perforation.* In our series of 1,816 cases of nonperforated acute appendicitis in which appendectomy was done there were 7 deaths, a mortality rate of 0.38 per cent. Schullinger<sup>14</sup> in his series of 886 cases has recorded a mortality rate of 0.33 per cent and Hawk and associates<sup>5</sup>, also during our present antibiotic period, has reported a mortality rate of 0.24 per cent in a group of 829 cases. Upon examination of table IV, which lists the causes of death in the nonperforated appendicitis group, several interesting facts are demonstrated. Although a free perforation of the appendix was not present in any of these 7 cases, it may be assumed that severe bacterial infection of the peritoneum was present in all cases at the time of appendectomy, since 3 of these cases had gangrenous appendices and in 2 there was evidence of severe local inflammation. In retrospect, we believe that it was unfortunate that a rubber drain was not placed

into the peritoneal cavity in the region of the cecum in these 5 cases. In 2 cases death was due to peritonitis and in 1 case to electrolyte imbalance and intestinal obstruction secondary to the marked local inflammatory process. Thus it would appear that, although appendectomy without drainage is still the preferred form of surgical therapy in acute nonperforated appendicitis, probably there are cer-

TABLE III

*The pathology and associated mortality rates in 1,984 cases of acute appendicitis 1947 to 1953 (St. Francis Hospital)*

Classification	No. Cases	Incidence	No. Deaths	Mortality
Abscess.....	36	1.8%	0	0.0%
Acute appendicitis without perforation.....	1,816	91.5	7	0.38
Acute appendicitis with perforation.....	132	6.7	8	6.06
Total.....	1,984	100.0	15	0.75

TABLE IV

*Causes of death in 1,816 cases of acute appendicitis without perforation (St. Francis Hospital)*

Fatal Complications	Age	No. Cases	Pathology at Surgery	Operation	Mortality
A. Medical					
Coronary occlusion.....	49	1	Acute diffuse	Appendectomy	
Cardiac failure.....	64	1	Subsiding	Appendectomy	
Cerebral vascular accident.....	81	1	Subsiding	Transurethral resection, appendectomy 7 days later	57.2%
Pulmonary embolus.....	31	1	Acute diffuse	Appendectomy	
B. Surgical					
Peritonitis.....	24	2	Gangrenous	Appendectomy	
Electrolyte imbalance & bowel obstruction...	69		Gangrenous & Carcinoma of colon	Appendectomy & ileotransverse anastomosis	42.8
Total or Average.....	53	7			100.0

tain instances in which bacterial contamination is so extensive and the infection so severe that drainage is necessary to allow escape of the massive quantity of purulent exudate formed.

It is clear that the majority of our fatalities were, in reality, due to medical complications related to the advanced age or physical status of our patients. The fatal *medical complications* encountered consisted of 1 case of acute coronary occlusion, 1 of cerebrovascular accident, 1 case of massive pulmonary embolism, and 1 case of cardiac failure. Since certain of these complications are at present

largely unavoidable, it would appear that the irreducible minimum mortality in nonperforated acute appendicitis should be approximately 0.25 per cent.

*Appendiceal Abscess.* Surgical opinion regarding the preferred treatment of appendiceal abscess is not unanimous. Cole and Elman<sup>2</sup>, in an early edition of their book, stated that, "the treatment of a definitely demonstrated appendiceal abscess should still be based upon fundamental principles of prompt appendectomy although the urgency is not nearly so great and delay for several days may be justified. On the other hand, nonoperative treatment for many weeks with an interval appendectomy later often involves a much longer period of convalescence than relatively prompt operation." In our experience, we encountered 36 cases of appendiceal abscess, 1.8 per cent of all cases studied. Among our hospital staff there was no unanimity of opinion with regard to the treatment of appendi-

TABLE V  
*The surgical treatment of 36 cases of appendiceal abscess\**

Therapy	No. Cases	Cases
Conservative (Interval appendectomy 2 to 6 mo.)	12	33.3%
Drained	13	36.1
Appendectomy	6	16.6
Appendectomy & peritoneal drainage	4	11.1
Appendectomy & drainage to peritoneum	1	2.9
Total	36	100

\* There were no fatalities in this group of cases.

ceal abscess. Conservative nonoperative therapy was carried out in 12 instances (33.3 per cent) when the inflammation proved was advanced, and the diagnosis relatively certain. When the diagnosis was less certain or the process was believed to be less clinically advanced, abdominal exploration was done. Appendectomy was done in 11 cases, but in 13 only drainage was possible. In none of our patients with appendiceal abscess was there a death (table V), but in 6 cases (16 per cent), there were subsequent complications. These complications were encountered only in the patients operated upon and consisted of fecal fistulas in 3 cases, mechanical obstruction in 1 case, and severe ileus in 1 case. The fecal fistulas in these cases healed spontaneously in from 16 to 57 days whereas the other complications noted were quite transitory. The absence of mortality in these cases may be due in part to the younger age of our patients which doubtless reduced the incidence of medical complications. Nevertheless, table VI suggests that when the diagnosis is relatively certain and when appendectomy is likely to be very difficult or impossible in the presence of an abscess, conservative or nonoperative therapy may be indicated. In our experience, this method of treatment was accompanied by the lowest incidence of complications and the shortest morbidity. However, uncertainty as to diagnosis, persistence of an unabsorbed abscess, threatened or actual disruption of the abscess wall, or mechanical obstruction must still remain as definite surgical indications.



The influence of the antibiotic agents upon appendiceal abscess would appear to be threefold. 1. Prior to the antibiotic era, appendiceal abscess was present in 25 per cent of all cases of appendicitis when first observed<sup>8</sup> yet our incidence of appendiceal abscess, 1.8 per cent, suggests that earlier diagnosis and therapy, perhaps in conjunction with prior symptomatic therapy with the antibiotic agents, is reducing this incidence. 2. It is also evident that the use of the antibiotic agents has made possible primary appendectomy in late cases of appendicitis with increased safety. 3. It is equally true that these same drugs promote more rapid resolution and absorption of appendiceal abscesses, without recourse to surgery, in a high percentage of cases and with a lower mortality rate so that the indications for primary appendectomy in appendiceal abscess certainly should not be extended simply because of the evident although limited protection offered by the present day antibiotic drugs.

TABLE VI  
*The incidence of complications of appendiceal abscess*

Therapy	No. Cases	Fecal Fistulas	Ileus Neurogenic	Mechanical Obstruction	Residual Abscess	Incidence
Drainage.....	13	3	1			30.7%
Appendectomy & drainage..	4				1	25.0
Appendectomy.....	6			1		16.6
Conservative (no surgery) ..	12					0
Total.....	36		6			16.0

*Acute Appendicitis with Perforation.* In 132 (6.7 per cent) of our 1,984 patients with appendicitis, an acute perforated appendix and peritonitis was discovered at the time of operation or at postmortem. Of these 132 patients, 128 were subjected to operation; of these 7 died, constituting an operative mortality rate of 5.4 per cent. Four patients were in such poor condition on admission that they were considered to be unacceptable anesthetic and surgical risks and therefore, were not operated upon. Of these 4 patients, 1 died shortly after admission with a subphrenic abscess and an associated empyema of the chest; the remainder survived. In common with most series, perforated appendices with peritonitis were noted most commonly in the younger and older age groups. Similarly, the mortality rate was highest in these same groups. In the former probably because of delay in diagnosis and in the latter because of the prevalence of the concomitant diseases so frequently present in the older age groups. The average age in the latter group was 62.3 years. The average survival period of the patients operated upon, which terminated fatally was 10.75 days.

Examination of the reasons for death in our 8 cases in the perforated appendicitis group shows that medical and surgical causes were about equal (table VII). The so-called *medical causes* responsible for death, were acute coronary occlusion, lower nephron nephrosis, which was spontaneous in 1 case and perhaps induced by associated sulfonamide therapy in a second, and alcoholism with acute cere-



bral edema in the fourth case. Our so-called *surgical causes* of death consisted of 1 case of residual abdominal abscess with rupture and generalized peritonitis, 1 case of evisceration associated with acute cardiac failure, 1 case of septicemia, and 1 case previously mentioned which was moribund upon admission and died of subphrenic abscess and associated empyema of the chest shortly after hospital admission.

TABLE VII

*The causes of death in 8 of 132 cases of acute appendicitis with perforation*

Cause of death	No. Cases	Av. Age	Day of Death Postoperative	Operation
Medical:				
Coronary occlusion.....	1	76	15	Appendectomy & wound drain
Toxic renal damage by sulfonamides & fecal fistula .....	1	52	17	Appendectomy & peritoneal drain
Lower nephron nephrosis .....	1	52	9	Appendectomy
Alcoholism-cerebral edema .....	1	50	7	Appendectomy & wound drain
Surgical:				
Abscess & peritonitis .....	1	88	13	Appendectomy & wound drain
Septicemia .....	1	2	5	Appendectomy
Evisceration & cardiac failure.....	1	68	5	Appendectomy
Subphrenic abscess & empyema (no operation).....	1	57	15	Moribund on adm. Died in 4 hours
Total.....	8	62.3*	10.75 (average)	

\* Exclusive of the single 2 year old patient.

The fatal and nonfatal medical complications presented by this group of 132 cases of appendicitis with perforation are summarized in table VIII. No single complication was pre-eminent and the total of medical complications did not exceed 10.6 per cent.

Table IX lists 38 surgical complications encountered in our 128 cases of acute appendicitis with perforations operated upon, an incidence of 38.6 per cent. Further analysis of these complications in relation to the operative procedure, and in particular with respect to the use of supplementary peritoneal drainage, proved most rewarding. When appendectomy only was done there was a 35.9 per cent incidence of complications, but when appendectomy was supplemented with peritoneal drainage there was an incidence of surgical complications of only 13.9 per cent even though there was a tendency to use the latter treatment in the more seriously contaminated cases. The advantage of drainage of the peritoneal cavity appears to be supported by the fact that when drainage was not used, there were residual pelvic abscesses for variable periods of time in 19 cases, wound

abscesses in 6 cases, ileus in 4 cases, and mechanical obstruction in 1 case. In contrast, when supplementary drainage was used, only 1 pelvic abscess was encountered, 1 case of ileus and 1 mechanical obstruction. Table X demonstrates rather decisively the importance of surgical drainage of the peritoneal cavity and not just the wound down to the peritoneum. It is perhaps only coincidental, but

TABLE VIII

*The fatal & nonfatal medical complications encountered in 132 cases of appendicitis with diffuse peritonitis*

Complication	No. Cases	Cases
Renal disease.....	3	2.2%
Pneumonia.....	2	1.5
Cardiac failure.....	2	1.5
Toxic encephalitis.....	2	1.5
Acute alcoholism.....	2	1.5
Septicemia.....	1	.75
Pulmonary embolus.....	1	.75
Premature labor.....	1	.75
Total.....	14	10.6

TABLE IX

*The incidence of fatal & nonfatal surgical complications in 128 cases of acute appendicitis with perforation treated by appendectomy with and without drainage*

Surgical Complication	Appendectomy and drainage (36 cases)	Appendectomy only (92 cases)
Pelvic or intra-abdominal postoperative abscess...	1	19
Wound abscess.....	0	6
Neurogenic ileus.....	1	4
Mechanical obstruction.....	2	2
Fecal fistulas.....	2	0
Incisional hernia.....	0	1
Evisceration.....	0	1
Total.....	5 (13.8%)	33 (35.9%)

the only incisional hernia, and the only instance of evisceration occurred in the cases in which drains were not utilized. It seems clear that failure to use a drain may well have been responsible for at least three *surgical deaths*, including the one in which perforation of a residual abdominal abscess terminated fatally.

Notwithstanding the fact that antibiotics have definite usefulness in the prophylaxis and therapy of infection, it is our opinion that the indications for drainage in perforated appendicitis are about the same now as when promulgated by Yates<sup>17</sup> in 1905. These indications are; a grossly infected or contaminated wound, an insecure intestinal closure, or a definite abscess cavity. It is well known that such drainage affects only a local area, but it affects *the* area of maximum

danger providing a means by which purulent or even fecal material may escape readily and with minimum danger to the abdominal cavity providing the drain is actually in contact with the source of trouble. Furthermore, where pooling of purulent material is prevented, the action of the antibiotic agents is most efficient, thus reducing both postoperative morbidity and mortality.

TABLE X

*The relationship of the surgical procedure to mortality rate in 128 cases of acute appendicitis with perforation*

Surgery	No. Cases	No. Deaths	Mortality
Drainage only.....	3	0	0%
Appendectomy with drainage of the peritoneal cavity.....	36	1	2.7
Appendectomy.....	82	4	4.7
Appendectomy with drainage of the abdominal wall.....	10	2	20.0
Total.....	128	7	5.46

N. B. During the period 1947 to 1950 the mortality rate was 7.1 per cent, but during the period 1950 to 1953 the mortality rate fell to 1.8 per cent.

## SUMMARY

The over-all mortality rate in 1,984 consecutive patients with acute appendicitis receiving antibiotics during the period 1947 to 1953 at St. Francis Hospital was 0.75 per cent.

Of 1,816 patients with acute appendicitis without perforation having appendectomy the mortality rate was 0.38 per cent. The majority of fatalities were ascribable to *medical* rather than *surgical* causes.

Of 36 patients with appendiceal abscesses treated without a death, 33.3 per cent had conservative treatment (i.e. no operation), 36.1 per cent had drainage of the abscess, and 30.6 per cent had appendectomy.

Of 132 patients having appendicitis with perforation there was an over-all mortality rate of 6.06 per cent. Half of these deaths were due to surgical and half to medical complications. There was an operative mortality rate of 5.46 per cent during the period 1950 to 1953. This mortality rate was reduced to 1.8 per cent. Nonfatal medical complications were present in 10.6 per cent and nonfatal surgical complications in 35.9 per cent of cases.

When peritoneal drainage was not used in appendicitis with perforation there were surgical complications in 35.8 per cent of the group but when appendectomy was supplemented with peritoneal drainage the incidence of surgical complications was only 13.9 per cent.

The use of the antibiotic agents does not alter our former indications for surgical drainage when there is gross infection or contamination, an insecure intestinal closure, or an abscess cavity.

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FURTHER EXPERIENCES WITH THE EXPERIMENTAL RECONSTRUCTION OF THE COMMON BILE DUCT: USE OF AUTOGENOUS AND HOMOLOGOUS, FRESH AND PRESERVED GRAFTS OF BLOOD VESSEL, URETER AND COMMON DUCT.\*

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In the past four years, experimental reconstruction of the common bile duct using fresh and preserved homologous and autogenous veins, arteries, common ducts, and one homologous ureter has been done in our laboratory on approximately 75 dogs. These experiments met with uniformly poor results due to the inability of the free tissue graft to withstand the necrotizing effect of canine bile.

Prior to 1949, all our experiments utilized fresh homologous and autogenous free tissue grafts. However, following the development by Gross and his associates<sup>2</sup> of a satisfactory physiologic solution for the preservation and storage of arteries, it seemed obvious and practical to apply this method to graft preservation for subsequent ductal reconstruction. At that time we had several long term survivals with fresh tissue grafts and we had not yet assured ourselves that free grafts, even though fresh, would not succeed. Furthermore, the use of preserved grafts presented a very practical advantage for the problem in man. Experimentally, the preservation technic gave us a bank of arteries and common ducts readily accessible for our work. It was also noted that the preserved grafts handled more easily and sutured better than fresh arteries and veins. It is the purpose here to report additional experiences with ductal reconstruction using fresh and preserved free tissue grafts. Our results with free vein grafts were reported previously<sup>4</sup>.

*Method.* Adult mongrel dogs weighing 10 to 20 kg. were anesthetized with intraperitoneal nembutal. A right rectus incision was made using sterile technic. The common bile duct was exposed; a segment distal to the cystic duct was excised, and a free tissue graft anastomosed to the ends of the common bile duct using a short polyethylene tube as an intraluminal splint. Although the distal end of this tube did not always extend into the duodenum, eventual passage into and through the gastrointestinal tract almost always occurred.

The grafts averaged 3 cm. in length. When the anastomosis was completed, the graft measured about 2 cm. in length. This was about one-half the length of the extra pancreatic common duct. No. 0000 catgut or no. 00000 arterial silk suture was used for the anastomosis. The abdomens were closed without external drains. Depopenicillin was administered routinely and subsequently as necessary.

Tissue grafts were preserved in Gross' solution. The solution was modified by

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FIG. 1. Microscopic section of a common duct graft preserved for 21 days prior to use. The animal died in 48 days. Necrosis and inflammation are evident.

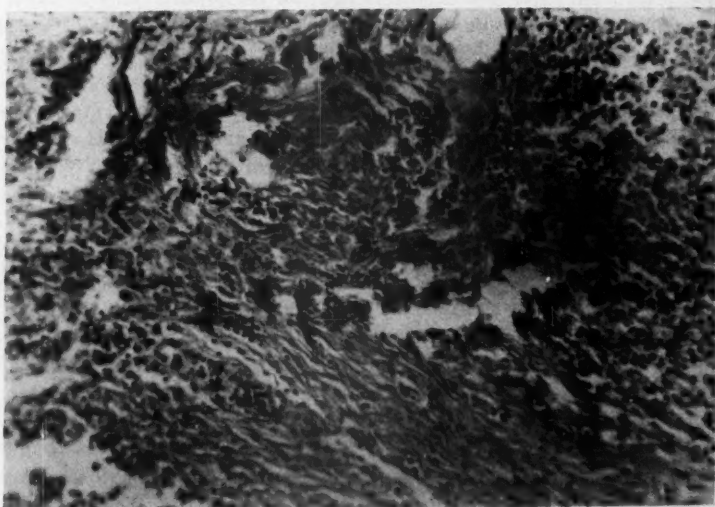


FIG. 2. Microscopic section of an arterial graft preserved 25 days prior to use. This animal died in 29 days. Extensive inflammation in the wall of the graft is present.

the addition of streptomycin, 1 Gm. per liter. A preliminary cholecystectomy with partial ligation of the common duct was done in 3 animals five weeks prior to the reconstruction. This was done to more closely simulate the condition



encountered clinically. In 1 of these 3 dogs, the reconstructive procedure was done transthoracically through the bed of the right ninth rib.

TABLE I  
*Controls*

No. of animals	Type of graft	Survival	Autopsy (gross)	Autopsy (micro)
2 #60	None. Duct transected and resutured	Killed 6 months	Normal c. duct	Normal c. duct
#61		Killed 6 months	Normal c. duct (peptic ulcer)	Normal c. duct
2 #58	Fresh homologous	11 days	Necrotic, anastomotic leak	Necrosis, bacterial invasion
#59		Killed 6½ months	Markedly narrowed	Fibrosis chr. inflam.
1 #64	Fresh autogenous	Killed 1 month	Normal c. duct	Mod. acute and chronic inflam.

TABLE II  
*Common duct grafts*

No. of animals	No. of days graft preserved	Survival	Autopsy (gross)	Autopsy (micro)
6 #54	Preserved 2 days	2 months	Complete obstruction	Necrosis. Inflam. obst.
#55	Preserved 4 days	2 days	Anastomotic leak	Necrosis. Marked inflam.
#66	Preserved 5 days	8 days	Breakdown both suture lines	Necrosis. Marked inflam.
#67	Preserved 7 days	1 month	Stenosis—supp. cholangitis	Necrosis. Marked inflam.
#49	Preserved 20 days	36 days	Anast. leak supp. cholangitis	Necrosis. Inflammation
#50	Preserved 21 days	48 days	Stenosis—supp. cholangitis	Necrosis. Inflammation

Some animals survived for periods up to six months. However, postmortem anatomic and microscopic studies of the reconstructed ductal system revealed uniform failure. Early failures were due to necrosis and perforation of the graft. Late failures were caused by fibrosis and stenosis of the graft with cholangitis

and suppuration (figs. 1 and 2). These findings are similar to those previously reported in our experiments using fresh venous grafts. The results are summarized in tables I to IV.

TABLE III  
*Homologous arterial grafts*

No. of animals	No. of days graft preserved	Survival	Autopsy (gross)	Autopsy (micro)
8 #56	Preserved 6 days	100 days	Complete obst. Ruptured ulcer	Inflam. obst. Peptic ulcer
#57	Preserved 7 days	25 days	Anastomotic leak. Fibrosis	Necrosis. Fibrosis
#42	Preserved 10 days	6 months	Complete obstruction	Necrosis. Inflammation
#43*	Preserved 17 days	2 months	Stricture, cholangitis. Ascites	Necrosis. Inflammation
#48	Preserved 19 days	68 days	Graft normal. Peptic ulcer	Marked inflam. Peptic ulcer
#51	Preserved 24 days	2 months	Stricture. Peptic ulcer	Inflammation. Peptic ulcer.
#52	Preserved 25 days	29 days	Necrosis and slough of graft	Necrosis. Inflammation
#53	Preserved 27 days	17 days	Complete slough of graft	Necrosis

\* Cholecystectomy with partial ligation of common duct performed 5 weeks prior to anastomosis.

TABLE IV  
*Ureter graft*

No. of animals	No. of days graft preserved	Survival	Autopsy (gross)	Autopsy (micro)
1 #47*	Preserved 15 days	28 days	Anastomotic separation	Acute inflammation

\* Cholecystectomy with partial ligation of common duct performed 5 weeks prior to anastomosis.

We noted that the right transthoracic approach as described by both Satinsky<sup>3</sup> and Humphreys<sup>3</sup> gave easy and excellent exposure to the porta hepatis and second part of the duodenum.

We have proved to ourselves that free tissue grafts, when placed in the biliary

ductal system, whether they are vein, artery, common duct or ureter, fresh or preserved, stand a poor chance for anatomic and physiologic success. A recent report<sup>1</sup> has emphasized the fact that canine bile exerts a strong necrotizing effect on suture lines. It seems apparent that there is a necrotizing effect on nonviable tissue, be it suture line or free graft.



FIG. 3. Specimen removed at nine months from the animal in which a vascularized vein graft was placed. The limits of the graft are indicated between markers. It can be seen that grossly there is little if any difference between normal common duct and graft.

In some instances a tab of omentum was wrapped around the free graft at the time of anastomosis in the hope that the vascularity of the graft would be enhanced and the chances of a successful *take* increased. It was our impression that the grafts thus wrapped withstood the effects of bile somewhat better than those not so protected. It therefore seemed logical to go one step further: to insert viable tissue grafts with an intact blood supply into common duct defects and note the effect of bile upon these. This was done on 1 animal—a pilot experiment

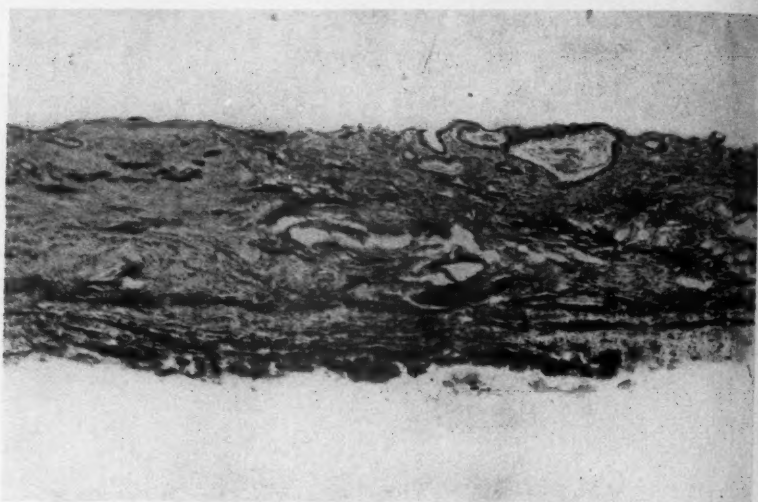


FIG. 4. Microscopic section of vascularized vein graft. The junction of normal common duct with its glandular epithelium and the vein wall with its flat endothelium is well demonstrated.

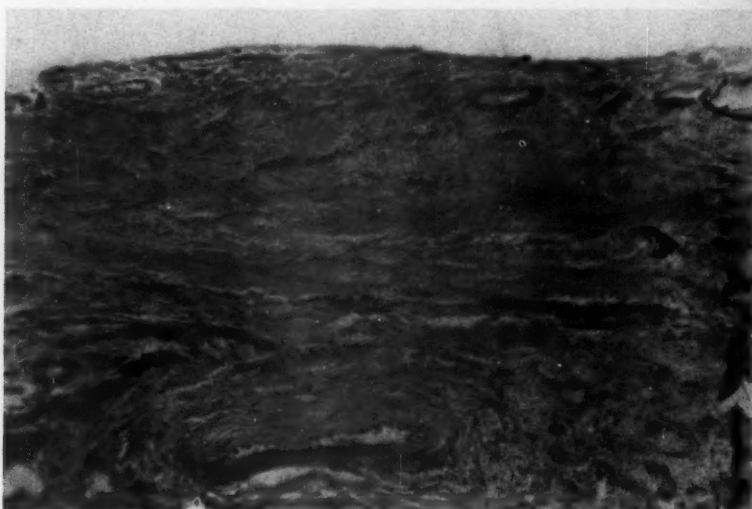


FIG. 5. Microscopic section through the wall of the vascularized vein graft shows under high power some hyalinization of the muscular coat. The endothelium however is preserved and active capillaries are present.

as follows: the first stage consisted of securing the jugular vein and anchoring it over a short length of polyethylene tubing. The vein and tubing were then wrapped in a section of the greater omentum and five weeks were allowed to

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elapse for vascularization of the vein. At the second stage the bile ducts were exposed through a transthoracic approach; a segment of the common duct was excised, and the vein with intact pedicle of omentum was swung up and anastomosed into the defect. This animal was killed at nine months. Clinically, the animal made an excellent recovery, he gained weight, had normal stools and urine, and showed no evidence of jaundice. Bromsulfalein and van den Bergh tests done just prior to killing the animal gave normal values. Grossly the liver, gallbladder, and bile ducts appeared to be normal. There was no evidence of obstruction or infection. Microscopic sections of the grafted area showed clearly the junction of normal biliary epithelium with the endothelial lining of the vein graft. Capillary vessels were seen in the vein wall indicating proof of vascularization (figs. 3, 4, and 5).

We have concluded that any tissue graft used to bridge a defect in the biliary ductal system must have an established blood supply and must be viable at the completion of the anastomosis. Before closing the book on tissue graft prostheses, we are encouraged to explore the problem further by using vascularized grafts. The technic of this operation has been worked out and is being applied on more animals.

#### CONCLUSIONS

Further experiments, using fresh and preserved free grafts for common duct reconstruction, confirm earlier reports of failure of this method.

Microscopic proof that bile is necrotizing to nonviable tissue is offered.

The right transthoracic approach experimentally offers excellent exposure to the common duct area.

This work, confirming failure of a general method of graft prosthesis has produced many technical details for consideration in a new two stage operation using a vascularized pedicle graft. The results of this procedure will be fully reported at a later date.

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## ACUTE APPENDICITIS IN CHILDREN\*

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Acute appendicitis, a condition which is usually diagnosed without much difficulty in adults, on occasion may present a clinical picture obscure enough to baffle the most astute physician. In childhood this is much more often true and the evaluation of children whose presenting symptom is abdominal pain will often be difficult and fraught with danger. Since children below the age of 14 years account for almost one-fourth of all the cases of appendicitis<sup>2</sup> the peculiarities of the disease in this group deserves careful study.

### ANATOMY

As is the case with adults, the location of the appendix will have a bearing on the symptomatology and findings. In children the location is even more apt to vary. Usually the appendix is found in the right lower quadrant and is directed either upward and medially toward the spleen or downward over the brim of the pelvis. It may be lodged behind the cecum pointing upward toward the right kidney. If the cecum is low, the inflamed appendix may come in contact with the bladder. It may also come in contact with the right ureter. When the cecum is low, the tip of the appendix may be located to the left of the lower end of the mesentery of the small intestine. On rare occasions, due to complete failure of bowel rotation, the appendix will be found on the left side. More often, due to incomplete bowel rotation or incomplete descent of the cecum, it will be found high on the right side under the liver and gallbladder. The appendix in a child has a wall which contains relatively less fibrous and more elastic connective tissue than that of the adult appendix.

The fact that a child's appendix is relatively longer as compared with the size of the peritoneal cavity; and the fact that the cecum is more mobile and the omentum shorter and thinner than in the adult is believed to result in less effective localization of the inflammatory process.<sup>6</sup> The younger the child the more important these factors become.

### ETIOLOGY

The most important etiologic factor in the pathogenesis of appendicitis is obstruction. This has been brought out by the work of Wangensteen, who was able to produce the pathologic and clinical features of appendicitis experimentally in animals and in surgical patients.<sup>5</sup> He and his co-workers have shown that the appendix has a definite secretory function and, when obstruction is present, it becomes analogous to a closed loop.

Appendiceal obstruction may be produced by different entities. Wangensteen

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demonstrated the presence of the so-called *Gerlach's mucosal fold* in 80 per cent of the cadavers he examined and he was also able to demonstrate the presence of a sphincter-like group of circular muscle fibers at the cecoappendiceal junction. These factors may produce some interference in the outflow of appendiceal secretions, but fecaliths appear to be by far the most frequent cause of obstruction. These concretions are present in a large percentage in all series of acute appendices where their presence is recorded. The actual incidence is probably much higher since it is likely that in many cases they are extruded into the cecum or into the peritoneal cavity by perforation before appendectomy is done.

In children infection with pinworms (*oxyuris vermicularis*) may produce appendicitis and it is believed that an infective process is initiated by obstruction produced by a bolus of pinworms.

Uttley<sup>8</sup> believes that sufficient obstruction to initiate the process which produces appendiceal infection can be produced by hyperplasia of the lymphoid tissue in the appendix and his evidence seems to indicate that this process is usually associated with more generalized lymphoid hyperplasia.

#### PATHOLOGY

When obstruction of the appendiceal lumen is established, the formation of appendiceal infection follows a definite pattern. Increased intraluminal tension produces anoxia with edema of the mucosa and hyperplasia of the lymphoid follicles. The next step is necrosis and ulceration of the mucosa. This usually takes place where the follicles approach the surface. Bacteria present in the luminal contents then penetrate the submucosa and spread rapidly in this layer inciting a diffuse inflammatory process. The infection then penetrates the muscularis by following the course of the blood vessels which pass through this layer and by entering the lymphatic channels. There is then a diffuse permeation of the subserosal layer. Venous congestion produces transudation of fluid into the peritoneal cavity and involvement of the serosa produces periappendicitis and spread of the infection to adjacent organs. Gangrene is caused by vascular thrombosis and results in necrosis and perforation. This usually occurs in the vicinity of a fecalith.

The series of events leading to perforation usually is much more rapid in children than it is in adults due to the anatomical peculiarities already mentioned. The wall of the appendix is relatively thinner than it is in adults; there is more lymphoid tissue which results in rapid absorption and spread of the infection and the wall of the child's appendix contains more elastic and less fibrous connective tissue. Of more importance is the fact that when perforation or penetration does occur, the localizing factors are much less effective than in the adult. This is due first to the fact that the more rapid establishment of perforation or penetration allows less time for the establishment of the localizing processes. Second, these localizing processes themselves are less efficient, due primarily, as has been mentioned above, to the relatively small thin omentum and the relatively large appendix. The increased mobility of the cecum is another anatomic factor which interferes with effective localization of the infection.

## SYMPTOMATOLOGY

In childhood eliciting the symptomatology is often more difficult than evaluating it. The child's story is colored by fear and reticence; the parent's story by emotion and apprehension. Children will communicate the fact that they have a pain and will indicate that it is in the abdomen but subjective localization will often go no further. The parents will be able to say that the patient has not felt well for the past few days and has complained of abdominal pain, but information as to the original location and subsequent migration of the pain; its character, and its variations in intensity usually cannot be obtained. If the history is such that the migration of the pain can be traced, it usually follows the same route that it does in adults, arising in either the epigastrium or periumbilical region and gradually migrating to the right lower quadrant. Since the localizing processes are less effective in childhood, a fair number of these patients, especially those under 6 years of age will be presented to the doctor complaining of generalized abdominal pain. The same is true in regard to abdominal tenderness. A finding peculiar to this group is the frequent presence of generalized abdominal tenderness without spasm. This is often found in the presence of perforation and generalized peritonitis and may be accompanied by distention, high fever, dehydration and other signs of severe toxemia.

In reviewing 100 consecutive histories of children under 12 years of age treated for acute appendicitis at the old Lakeview and the Louise Obici Memorial Hospitals we found that in the group below 6 years of age, right lower quadrant pain was present in 62 per cent. In the group between 6 and 12 years of age, lower quadrant pain was present in 78 per cent of the patients. Right lower quadrant tenderness was present in 90 per cent of the group under 6 years of age and in 95 per cent of the group over 6 years of age. Localized right lower quadrant spasm was present, in 67 per cent of the patients under 6 and in only 57 per cent of those between 6 and 12 years of age. On rectal examination there was right side tenderness in 78 per cent of the younger group and in only 70 per cent of the group over 6 years of age. Fever over 100 F was present on admission in 62 per cent of the younger group and in 46 per cent of the older group. Peritonitis without any definite localization was present in 19 per cent of the younger group and in only 7 per cent of the older group. Perforation occurred in 38 per cent of the group under 6 and in 10 per cent of the group over 6 years of age. Localized abscess formation was present in .05 per cent of the younger group and in .09 per cent of the older group. Ten per cent of the younger group had mesenteric adenitis and 13 per cent of the older group had mesenteric adenitis. There were two deaths in the series and both of these were in the younger group, making the mortality rate in this group 10 per cent or 2 per cent for the whole series. Both of the deaths occurred in children who were extremely toxic and had temperatures over 105 F. on admission with generalized distention without any localization. Both had perforated appendices and generalized peritonitis.

This series is a small one and statistics based on such series are apt to be misleading if taken literally. However, they do correspond fairly well with the statistics gathered from larger series and emphasize very definitely the increased

difficulties encountered in the younger group and the increased seriousness of the disease in this group.

In addition to realizing that there may be no localization of tenderness in children with appendicitis it is important to remember that the point of tenderness may not be in the usual location. As mentioned above, the position of the appendix varies much in childhood. The retrocecal appendix may produce pain and tenderness in the right loin and by effecting contraction of the iliopsoas muscle may produce contraction of the right hip. When, through failure of descent of the cecum, the appendix lies high in the right side of the abdomen, maximum pain and tenderness may be found in the right upper abdominal quadrant. These patients will usually have early vomiting.

When the appendix lies to the left of the mesentery of the small intestine the localizing signs will be present in the midline. When the organ is located low in the pelvis, it may cause irritation of the bladder producing frequency of urination or irritation of the rectum producing diarrhea. If it comes in contact with the right ureter, pyuria will usually be encountered.

Rectal examination will often be of great value and will at times establish localization when this cannot be done by abdominal palpation. Here, even more than in examination of the abdomen, extreme gentleness is mandatory. Just as it is wise, in examining the abdomen, to start in the left lower quadrant and work around to the right, so in rectal examination it is advisable to palpate on the left side first and then determine whether the opposite side is more sensitive. It is important to distinguish between the discomfort or pain which is caused by the palpating finger tip and that which is produced by dilatation of the anal sphincter.

Routine laboratory work will usually reveal a leukocytosis of over 10,000 per cu. mm. and there will usually be a fairly marked shift to the left.<sup>4, 7</sup> Urinalysis is important as an aid in determining the state of the patient's hydration by the presence or absence of acetoneuria and for indications of urinary infection.

#### DIAGNOSIS

In late childhood appendicitis is usually not difficult to recognize. In infancy and early childhood, however, this is not the case. In the group under 6 years of age, the imperfect history and the lack of localizing physical signs may make diagnosis extremely difficult. It is necessary first of all to consider the diagnosis of appendicitis in any child with abdominal complaints. The triad of symptoms; abdominal pain, vomiting and fever should be considered appendicitis until proved otherwise. When these symptoms are present and the diagnosis is in doubt, the patient should be hospitalized and physical examinations and laboratory work should be frequently repeated. The importance of frequent examination has been stressed by many authors. When this routine is started early some right lower quadrant localization, either on rectal or abdominal examination, will almost invariably show up before perforation occurs.

The patient who presents the above triad of symptoms together with generalized tenderness and signs of severe toxemia cannot be treated expectantly. If

there is no other obvious cause of the abdominal findings, these patients should be operated upon for appendicitis as soon as they can be prepared for surgery.

In evaluating the cases which do not present the above triad of symptoms, abdominal pain is the most constant symptom appearing in over 95 per cent of all patients.<sup>4, 7</sup> Pain with localization in the right lower quadrant should establish the diagnosis if no other cause can be found. Over 80 per cent of children with acute appendicitis vomit and less than 10 per cent have urinary complaints.<sup>4, 6, 7</sup>

There is no way of differentiating between acute appendicitis and mesenteric adenitis with any degree of certainty.<sup>8</sup> When the onset has been accompanied by high fever and when an upper respiratory infection is present, mesenteric adenitis should be suspected, but there can be no certainty about the diagnosis. When the diagnosis is in doubt, operation should be done. Careful study will usually result in an accurate diagnosis, especially when the early, doubtful cases are followed by frequently repeated examinations. However, when doubt persists, after all efforts to resolve it have been made, operation should be done.

#### TREATMENT

The treatment of acute appendicitis in childhood, as in adult life is appendectomy. This holds true whatever may be the stage of the disease. While there are some who still may contest this latter statement in regard to adults, its application in the treatment of this disease in childhood is almost universally accepted. The impaired localizing powers of a child's peritoneal cavity make conservative treatment, even of an appendix which has been ruptured for some time, an extremely hazardous procedure.

We do not believe in the use of drains at operation except in the presence of localized infection and in such instances they are limited to the treatment of appendiceal abscess. It has been shown experimentally that a drain becomes walled off within a few hours after its insertion so that drainage is only effective in a small area around the tip of the drain. Hence, it is futile to attempt to drain the entire peritoneal cavity or even the entire right lower quadrant.

In the treatment of appendiceal abscess drainage is effected and the appendix is removed if this can be done without breaking down the localizing processes which have become established. If this cannot be done, the appendix is left in and removed at a later date.

A McBurney incision is the incision of choice and is used for all cases except when an ectopic location of the appendix would make it impractical.

Postoperative treatment is of primary importance and will have a great influence on the mortality and morbidity rates. It cannot be adequately discussed here but a few general remarks may be in order. We believe that simplicity should be the keynote and that only those procedures which have a definite indication should be used. In the ordinary uncomplicated case the patient will be able to take food and liquids and to be ambulatory within 24 hours. The routine use of gastric suction in these patients is not necessary, but this procedure should be used at the first sign of postoperative distention or persistent postoperative vomiting. Preoperative restoration of fluid and electrolytic balance and postoperative maintenance of this state are extremely important.



Without debating the advisability of taking cultures in all cases, we believe that antibiotics with the widest possible spectrum should be given. This requirement is fulfilled by penicillin given in combination with streptomycin or by aureomycin or terramycin. Wright<sup>9, 10</sup> and his co-workers, in a series of articles, found that these antibiotics were the most effective for use in the treatment of cases of peritonitis. As a matter of practical expedience we use penicillin in combination with streptomycin in the less severely infected cases until medication can be taken by mouth and then terramycin is substituted. In the severely infected cases terramycin is given intravenously, from the start.

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## OBSTRUCTIVE ENTEROSTOMY IN THE TREATMENT OF OBSTRUCTION OF THE SMALL BOWEL

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While medical literature shows that the mortality rate from acute obstruction of the small bowel is still high, there has been a decided lowering of the mortality rate during the past 10 years. For instance, in a report by Paul Nemir, the death rate at the University of Pennsylvania Hospital for the 10 years from 1940 to 1950 was 10 per cent and a number of surgeons have reported mortality rates of from 7 to 8 per cent. Many observers, however, still report mortality rates of from 12 to 20 per cent.

When one takes a retrospective view of what the mortality rate was in the early years of this century, when it varied from 25 to 75 per cent, one can truly visualize the marked improvement that has taken place in the results of treatment of obstruction of the small bowel. The investigations of numerous men, beginning about 1930, have served to clarify the cause of death in high obstructions of the small bowel as being due to *dehydration* and the *early loss of electrolytes*. In low obstructions of the small bowel death is evidently due to some other cause for there is not the loss of the electrolytes nor the water loss that had been found to be so detrimental in high obstruction. The type of obstruction, whether simple, loop or strangulated, also plays a different role, with complicating factors such as shock, hemorrhage and infection.

In the earlier years of my surgical practice (from 1907 to 1927) we were convinced that the contents of the obstructed bowel were lethally toxic and when released into healthy bowel usually caused death. We still hold this view.

Gatch, Wangenstein, and others have proved, to their satisfaction, that the contents of the obstructed bowel are no more toxic than the contents of the normal bowel. I cannot subscribe to this view. In my earlier surgical practice, I saw too many patients die promptly when an obstruction was relieved and the contents of the obstructed bowel were emptied into healthy bowel. Death occurred with high temperature, rapid pulse, and delirium usually within 10 to 12 hours.

Myers and his co-workers have isolated a substance from the contents of obstructed bowels, lysozyme, which produces the same pathologic picture in the mucosa of the bowel as does intestinal obstruction. Light of Vanderbilt University has substantiated their findings. However, whatever it is, I am convinced there is present a lethal toxic agent in the contents of the obstructed bowel, which is not absorbed by the mucosa of the obstructed bowel but is rapidly absorbed after entering healthy bowel. I vividly recollect a 6 year old child who was operated upon on Aug. 16, 1912 for an intussusception which was easily reduced.

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This child left the operating room in excellent condition, but was dead within 12 hours with all of the symptoms of a severe toxemia, high temperature, rapid pulse and delirium. Only recently a colleague of mine was discussing the case of a child with a strangulated hernia and asked me how I could account for its death. There was practically no trauma, the bowel was viable, and he was able to reduce the hernia at operation without difficulty. The operation was done about 8 p.m. and by 7 o'clock the next morning the child was dead. This occurred in the year 1950 and was a repetition of the same old story which we had in the early surgical intervention of acute obstruction of the small bowel.

Shortly after having the experience referred to with the intussusception, I was in the late Doctor Albert Ochsner's clinic when he presented a case of acute obstruction of the small bowel which he treated by relieving the obstruction and introducing a Monk's tube about 3 feet long upon which he threaded the bowel completely emptying the bowel. He closed the opening in the bowel with the remark that there would be no question as to the patient's recovery. I practiced this method of treatment for several years with a decided lowering of the mortality rate, but on account of the trauma incident to the introduction of the tube, I discontinued its use and began to introduce the end of a large rubber tube into the bowel and milk the contents out through the tube. However, there was too much trauma associated with this as was with the other procedure and with the last patient upon whom it was used I underestimated the bursting strength of the bowel and ruptured it. Notwithstanding the teaching of the doctrine that *the contents of the obstructed bowel are no more toxic than those of the healthy bowel*, my observation has been that the proponents of this view always empty the obstructed bowel with various devices claiming that it is done to relieve intraluminal tension and promote the return to normal of the circulation.

By 1927 I had become convinced that so long as the bowel was obstructed there was little or no absorption from it and we began to put this fundamental principle into operation. We do what we have termed an obstructive enterostomy. This we have done in conjunction with the use of a Levin's tube as advocated by Matas in 1924 and the use of oxygen intranasally as suggested by Fine, and the maintenance of the blood plasma, blood electrolytes and water level of the blood. Our mortality rate from 1927 to 1949 dropped to 7 per cent in 113 cases. I believe that we owe much to Wangensteen, Dott, Sperling, Dragstedt, Gatch, not to mention many others, who have done so much to clarify the pathologic, physiologic and anatomic changes which take place in obstruction of the small bowel. Especially do I believe that Sperling, in 1938, reported one of the most comprehensive experiments upon acute obstruction of the small bowel. This work has clarified many facts which I, as a country surgeon, had already learned from clinical experience and taken for granted; the most important of which was that *absorption from an obstructed bowel is held in abeyance from the beginning of obstruction*.

Sperling's investigations embraced the *intra-enteric pressure in acute simple obstruction of the small bowel; the effect of acute obstruction upon the bowel wall; its influence upon the tensile or bursting strength of the bowel; the influence of simple*

*obstruction and increased enteric pressure upon the bowel function; its effect upon intestinal secretion; the effect of obstruction and increased enteric pressure upon intestinal absorption; and the effect of prolonged distension upon the structure, viability, and permeability of the bowel wall.* After a full discussion of each phase, he sums up his conclusions as follows: "The changes described may be summarized in the following manner. With the onset of intestinal obstruction there is stasis of fluid and gas within the bowel. The stasis produces a slight increase of intra-enteric pressure and a moderate degree of distension which stimulate the normal bowel to increased peristalsis. Distension and increased intra-enteric pressure result in an augmented secretion of intestinal juices which add to the content of the bowel. Absorption is decreased early in the course of the obstruction. There is thus a progressive increase of distension and intra-enteric pressure. With a rise in intra-enteric pressure there is eventually manifested interference with the circulation of blood in the wall of the intestine. Venous stasis ensues and causes infiltration of the intestinal layers with leukocytes. Eventually hemorrhagic infarction, necrosis, and even perforation of the intestine may take place. If the intra-enteric pressure is maintained over a sufficient length of time the viability of the wall of the bowel becomes impaired and its permeation by toxic material may take place in the gangrenous patches. Death is then due to peritonitis or to absorption of toxic material by way of the peritoneum. Relatively low pressure (20 to 30 cm. of water), if maintained over a sufficiently long period (17 to 30 hours), produces structural changes in the intestinal wall which will allow this to take place."

With the exception of the toxin present in obstruction of the small bowel and the marked increase of bacteria in the contents of the bowel, particularly those of an anaerobic character, Sperling's investigations give a clear, concise, lucid explanation of all of the pathologic, physiologic and anatomic changes which take place.

Eleven years prior to Sperling's investigations, we had become convinced that absorption from the obstructed bowel was held in abeyance; that an enterostomy, so constructed as to prevent the contents of the obstructed bowel from entering healthy bowel—contents to be emptied through the enterostomy tube upon the surface of the body—eliminated the danger of absorption of toxic material. We had also, by repeated cultures, determined that there was a marked increase of anaerobic organisms in the contents of the obstructed bowel and for that reason we applied the principle, of the open wound treatment of the potentially infected abdominal wound. Several years ago in a paper presented before the Southern Surgical Association, I reported 12 cases of spreading gangrene of the abdominal wall, 8 of which had obstruction of the small bowel. After using the open wound treatment this complication was almost completely eliminated. Only once—and that was four years ago—have we had spreading gangrene of the abdominal wall associated with obstruction of the small bowel.

By obstructive enterostomy is meant the introduction of a tube,  $\frac{1}{2}$  inch in diameter or larger—possibly as large as 1 inch in diameter—into the distal end of the obstructed bowel—after the obstruction has been released—in such a manner

as to partially intussuscept the bowel so as to completely close it off from the healthy bowel and prevent any of its contents from entering the healthy bowel. The enterostomy tube is brought to the surface of the body through a stab wound.

Reduction of the intraluminal pressure is the key to restoration to health of the affected bowel. The prevention of the contents of the obstructed bowel from entering healthy bowel and the relief of intraluminal tension are the two most important factors which have reduced the mortality rate in the present series of 183 patients treated from Jan. 1, 1940 to present date. There were deaths or a mortality rate of 3.8 per cent.

Another one of the great advantages in this operation is that there is a minimum amount of trauma inflicted upon the affected bowel. The entire bowel is not handled. The obstruction is sought for and released without traumatizing any other section. If the bowel is viable all that is necessary is the construction of the obstructive enterostomy. If the bowel is not viable the same operation is indicated after resection of the nonviable portion. The technic of the operation is simple. Where resection is not indicated the obstructed bowel is tied off at the obstruction with a fine rubber band,  $\frac{1}{16}$  inch in diameter. About 8 inches of the bowel are then milked backward to empty it and another rubber band is applied. We prefer small rubber bands to clamps as they cause far less trauma and are much more effective in protecting the wound from spillage. A purse-string suture of fine linen is then inserted upon the anti-mesenteric border of the bowel; an opening is made in the bowel; the rubber tube is introduced; the purse-string suture is tied and fastened to the tube and retied. A second purse-string suture is then placed about  $\frac{1}{2}$  inch above the first and the bowel wall partially invaginated and the suture is tied. The tube is passed through a stab wound to the surface of the abdominal wall. If practicable omentum is interposed between the bowel and abdominal wall. If this cannot be done the bowel is pulled snugly up to the abdominal wall. The rubber bands are then cut and removed. If resection is necessary, an end to end anastomosis should be made.

When the tube is opened there is at first usually a free flow of intestinal contents. This stops after a few minutes and usually does not begin again for at least 30 hours or longer. I have seen it wait for 96 hours before starting again. The large enterostomy tube, in conjunction with Wangensteen decompression and oxygen intranasally, relieves the gaseous distention of the bowel; lowers the intraluminal pressure; ultimately the circulation becomes re-established; peristalsis is initiated and the contents of the bowel are evacuated.

I will not claim that the delay in bowel function did not cause me uneasiness. In the early years of our adoption of this procedure it often caused me much worry before I had become thoroughly convinced that there would be no absorption from the obstructed bowel. We gave antuitrin or pitressin or prostigmine; or attempted to wash out the loop with saline solution without any appreciable results so far as evacuation of the bowel contents were concerned. I once even reopened an abdomen to see if another obstruction had occurred or if I had inadvertently introduced the tube into the distal segment of bowel instead of



the proximal. Ultimately, after the restoration of the circulation, peristalsis is re-established.

In the closing of the operative wound we invariably use the open wound technic which I have long advocated in the treatment of potentially infected abdominal wounds. It matters not how meticulously careful one's technic is, one is dealing with a structure in which anaerobic organisms are teeming and it is practically impossible to prevent contamination of the wound. Leaving the wound open without dressings is a sure way of preventing any fulminating type of anaerobic infection.

When acute intestinal obstruction is diagnosed a duodenal tube is introduced and Wangensteen decompression is instituted as early as possible. Regardless of the blood picture, in intestinal obstruction of either the upper small bowel or lower small bowel, we administer 5 per cent glucose in physiologic sodium chloride solution intravenously and also give a blood transfusion. As soon as the patient's condition justifies it he is transferred to the operating room and ordinarily is given another transfusion during the operation in addition to the continuation of the glucose and saline solution.

Postoperatively the water level of the blood is kept as near normal as possible and the blood electrolytes and blood plasma are kept replenished. Oxygen intranasally is kept up continuously until peristalsis is re-established. The obstructive enterostomy tube, combined with Wangensteen decompression, and the continuous administration of oxygen keeps the intraluminal pressure lowered; prevents anoxia of the bowels; promotes the re-establishment of the circulation and ultimately peristalsis.

#### DISCUSSION

The operation of obstructive enterostomy is based upon the soundest of surgical and physiologic principles. One need have no fear that the patient will succumb to the absorption of toxic material from the bowel. Absorption is held in abeyance practically from the beginning of the obstruction.

Autopsies were obtained upon 3 patients. One, a strangulated umbilical hernia, in which 18 inches of gangrenous bowel were resected, showed thrombosis of the pancreaticoduodenal artery with complete devitalization of the duodenum. There was no peritonitis and the site of resection was perfectly healed. In 1 case of resection the gangrenous condition had extended further and it, combined with peritonitis, was the cause of death. In a third, at the site of obstruction the bowel was gangrenous and there was some spillage of bowel contents. This patient died of peritonitis. In a fourth there was a history of 96 hours duration of obstruction before admission. She was given blood transfusions and 5 per cent glucose with saline solution intravenously, Wangensteen decompression and oxygen continuously. Six hours later there was very little improvement. She died five hours after operation. No autopsy was available upon the other 3 patients. One of these died of acute postoperative lobar pneumonia. The 2 other deaths were within 48 hours following operation. One was a diabetic and 1 had suppression of urine or renal failure.

While we believe that the restoration of blood plasma, and blood electrolytes; the continuous Wangensteen decompression; the continuous administration of oxygen intranasally; and the open wound treatment all contributed to the maintenance of this low death rate, the most important factor has been the operation of obstructive enterostomy.

It has been said that we must have a large percentage of operations for secondary closure of the enterostomy wound. As a matter of fact, we have never had to close one. Usually by the fourth day following removal of the tube, which is done about the seventh postoperative day, drainage has ceased.

I have frequently seen the statement made that enterostomy in the treatment of acute obstruction of the small bowel was a futile gesture. I grant that as I have often seen an enterostomy made with a small catheter or small tube introduced into the side of an obstructed bowel by the Witzel technic, such an operation is both futile and useless. However, when one uses a tube not less than  $\frac{1}{2}$  inch in diameter or larger and partially invaginates the obstructed bowel so that its contents cannot gain access to healthy bowel, it is the simplest and most effective measure we have in our surgical armamentarium for saving the life of one suffering from acute obstruction of the small bowel from whatever the cause.

#### SUMMARY

These 183 cases embraced all forms of obstruction. There were strangulated hernias with viable and nonviable bowel, volvulus, strangulated loop obstruction and obstructions due to adhesions.

#### TYPES OF OBSTRUCTION

1. Obstruction due to adhesions with viable bowel, release of obstruction and obstructive enterostomy. There were 66 negro patients with one death and 33 white patients with one death, a total of 99 patients with two deaths.

2. Strangulated loop obstruction and obstruction with gangrene necessitating resection. There were 19 Negro patients with two deaths and 2 white patients with no deaths making a total of 21 patients with two deaths.

3. Strangulated inguinal hernia with viable bowel. There were 20 Negro patients with no deaths and 1 white patient with one death, or a total of 21 patients with one death.

4. Strangulated inguinal hernia, gangrene of bowel with resection. There were 4 Negro patients with one death.

5. Ventral hernia (postoperative). There were 3 Negro and 2 white patients with no deaths.

6. Internal hernia. There was 1 white patient without a death.

7. Femoral hernia with gangrene of bowel and resection. There were 2 Negro and 2 white patients with no deaths.

8. Intussusception. There were 6 Negro and 1 white patients with no deaths.

9. Volvulus with viable bowel. There were no deaths in 7 Negro and 5 white patients.

10. Volvulus with gangrene and resection. In this group there were 5 Negro patients with no deaths.

## CONCLUSIONS

While the death rate is naturally higher where gangrene has supervened, we believe that the type of operation here described is in most cases preferable except where a Mikulicz type of operation is indicated.

The mortality rate of 3.8 per cent consistently maintained over a period of 12 years is the lowest that I have been able to find recorded in current medical literature.

We believe that while the low mortality rate is largely due to the operation of obstructive enterostomy, it is important to emphasize the open wound treatment; the maintenance of electrolytes in the blood; blood transfusions, Wangenstein decompression; and the continuous administration of oxygen; all play a part in the treatment of acute obstruction of the small bowel.

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## INDICATIONS AND CONTRAINDICATIONS FOR TONSILLECTOMY\*

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If the function and the pathologic processes occurring in the lymphoid tissue known as the tonsil and the adenoid were fully known, the surgical management of this tissue could be more intelligently managed. Until this knowledge is obtained, the surgeon should assume that normal, healthy tonsils and adenoids serve a useful purpose. It is now generally accepted that the lymphoid elements in the pharynx and nasopharynx play an important part in the development of immunization in the young child.

There are certain facts which suggest that this lymphoid tissue is directly concerned with the defense of the respiratory tract against invading micro-organisms. The maximum development of the tonsils and adenoids coincide with the period of establishment of relative immunity to respiratory infections. Vital staining methods have demonstrated active cellular defense against bacterial invasion of the tonsil.<sup>8</sup> The importance of this defense mechanism of the sub-epithelial lymphatic structures in autovaccination is stressed by Digby.<sup>2</sup>

Investigators<sup>4</sup> working on the role played by the secondary nodules of the tonsils under normal and abnormal conditions further strengthen the defense theory.

The simultaneous infection of both tonsils by the streptococcus, the course of infection and the usual absence of local complications have led many to believe that acute tonsillitis is not a local but a systemic disease. This theory was first advanced by Fein<sup>3</sup> as early as 1921.

There seems to be little doubt that under certain conditions the pharyngeal lymphoid tissue may act as a focus of infection. Fein's theory may account for the fact that tonsillectomy may not produce desired results in patients with rheumatic fever, nephritis and arthritis.

In 1912, Billings<sup>1</sup> made the medical profession conscious of focal infection. Unfortunately, in many instances, this theory has been carried too far, even to the point of considering this lymphoid tissue as useless and that its prophylactic removal could result in no harm to the individual.

### INDICATIONS

Although tonsillectomy will lower the incidence of *sore throats*, it apparently does not have any beneficial influence on recurrent attacks of rheumatic disease, glomerulonephritis and rheumatoid arthritis. Hypertrophic arthritis is probably a degenerative disease and appears to have no relationship with upper respiratory

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infections and no improvement in symptoms may be expected following tonsillectomy.

Although the number of recurrences of acute rheumatic fever appear not to be influenced by tonsillectomy, the mortality rate is distinctly higher in children whose tonsils have not been removed.<sup>7</sup>

It is generally accepted that acute systemic disease may occur secondarily to acute tonsillar infections. In the absence of a scientific basis for the selection of cases for operation, the surgeon must rely upon his past experience and judgment. He should know that there is no evidence of infection to be found elsewhere. The procedure should be delayed until systemic disease is quiescent and the patient fortified with chemotherapeutic and/or antibiotic drugs before the operative procedure is attempted.

The effect of tonsillectomy on respiratory infections in 2,200 children was studied by Kaiser<sup>8</sup> over a period of 10 years and compared with a similar group in which tonsillectomy was advised but for various reasons the procedure was not done. It was found that tonsillitis occurred in approximately 38 per cent of the cases. There was a marked decrease in the incidence of this complaint as

TABLE I  
*Effect of the tonsils on outcome of rheumatic infection in 597 children*  
(Followed for 10 years)

	No. of Cases	Died	Recurred	No Recurrence
1. Remained in . . . . .	156	13%	46%	41%
2. Out at 1st attack . . . . .	187	7%	48%	45%
3. Out after 1st attack . . . . .	254	4%	44%	52%

compared with the control group over the 10 year period. As far as the common cold was concerned, the operative group showed no significant advantage over the nonoperative group. The incidence of purulent otitis media was considerably lower in the operative group for the first three years following the operation. The beneficial results in these cases can probably be attributed to the adenoidectomy. Favorable results were obtained in the group complaining of cervical adenitis in which a tonsillectomy had been done, but no improvement was noticed in patients having sinusitis, nasal allergy or laryngitis. While tonsillectomy appeared to decrease the incidence of upper respiratory infection, there was an increase in lower respiratory symptoms in the operative group.

Although allergy is not a contraindication for tonsillectomy, it must be remembered that the tonsils are often involved in the generalized upper respiratory lymphoid hyperplasia that is frequently associated with this condition. When it is necessary to remove the tonsils, the operation should not be done during the active phase of an allergic state.

Such conditions as pharyngitis, unexplained fevers, and failure of the child to gain weight are occasionally benefited by the removal of the tonsils. There does not appear to be an adequate explanation for the beneficial results obtained.

Benign and occasionally malignant neoplasms involving the tonsil often re-

quire the removal of this structure to effect a cure. This is particularly true of cysts, aberrant salivary gland tissue, solitary giant cell folliculoma and an occasional lymphosarcoma.

#### CONTRAINDICATIONS

Since tonsillectomy in both children and adults may be followed by a number of serious consequences, no person should be subjected to this procedure unless careful and adequate study indicates that the tonsils are diseased and are likely producing injury to the person's health.

An adequate physical examination and laboratory studies should be done to rule out local and general conditions which would make operation or an anesthetic a dangerous procedure. Special attention should be given to the pulmonary, cardiac, genitourinary and blood systems.

The relationship of tonsillectomy and poliomyelitis has received considerable publicity within recent years. Extremes of opinion exist regarding this relationship. Analysis of the literature on this subject suggests that the incidence of poliomyelitis is not increased by tonsillectomy, but it would appear that children developing the disease within a few weeks after operation are more likely to have the bulbar type. With our present knowledge it is probably not wise to do tonsillectomies during an epidemic of poliomyelitis or other acute contagious diseases.

The work of Herndon and Jennings<sup>5</sup> on the susceptibility to poliomyelitis emphasizes that the paralytic form has both a genetic and environmental component. Both of these factors should be simultaneously evaluated when tonsillectomy is contemplated in children.

#### CONCLUSIONS

From the foregoing discussion it appears obvious that the otolaryngologist is confronted with a complex problem regarding the tonsil question. Until proved otherwise, the following can be considered as indications for surgical intervention:

1. Frequent attacks of acute tonsilitis with or without associated complications.
2. In certain cases of focal infection.
3. In local pathologic states as obstructive hypertrophy, peritonsillar abscess and new growths.

The contraindications consist of those conditions or circumstances which would render operation an undue risk to the patient.

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## SUBDELTOID BURSITIS

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Bursitis is a word which is becoming known to and used by the layman almost as much as such words as neuritis, arthritis and colitis. Any pain or stiffness in the region of a joint, especially the shoulder joint, which is the most common site of bursitis, is often diagnosed by the layman as bursitis. This diagnosis is also often made by the physician for the same symptoms, without making a careful examination.

The painful shoulder has become a complicated syndrome. This is evidenced by the large number of discussions given and articles written on the subject. Such conditions as bursitis, tendinitis, arthritis, periarthritis, ruptured disk, scalenus anticus syndrome, and the shoulder-hand syndrome are encountered in the differential diagnosis.

Subdeltoid or subacromial bursitis is a common condition and a common cause of the painful shoulder. Closely associated with this condition is a peritendinitis and calcified peritendinitis. A primary subdeltoid bursitis is probably unusual. It is usually secondary to a tendinitis of the musculotendinous or rotator cuff which forms the floor of the bursa. I have seen 1 case reported by a pathologist as subdeltoid bursitis.

Sixty per cent of my cases of subdeltoid bursitis and tendinitis were in women. The conditions usually occurred in those people engaged in some active physical activity but not in those of strenuous activity. People engaged in occupations such as mill workers, shipping and mailing clerks, typists and active house work were most often affected. Chronic trauma is the cause.

The differential diagnosis between subdeltoid bursitis and tendinitis in the chronic stage may be difficult. Roentgenograms taken in different views will reveal calcification if it is present. The size of the calcification does not necessarily correspond to the patient's symptoms. We see roentgenograms of chests, and other parts of the body revealing the shoulders, showing large calcifications in the shoulder regions although the patients have no shoulder symptoms. Nevertheless a patient with a very acute shoulder condition may have a rather small calcification. Recently the neurotic and psychoneurotic symptoms which may develop in a patient with chronic painful shoulder have been emphasized. These symptoms add greatly to the difficulty in making a diagnosis and in prescribing treatment for the patient with chronic shoulder pain. Usually these patients recover after long periods of time with conservative treatment.

Included in the conservative treatment is the treatment of the patient's general condition by roentgenotherapy, physiotherapy, and psychotherapy if indicated. I do not include in the treatment the extraction of all the patient's teeth without very positive indication. I have seen 2 patients recently in their

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early thirties who had had all their teeth extracted, by advice of their physicians, for chronic shoulder conditions. Neither had made improvements.

My purpose in presenting this subject is to outline my observations of the diagnosis and treatment of acute subdeltoid bursitis and tendinitis. These conditions are easy to diagnose in the acute stage. They occur most frequently in patients in their thirties. Usually the patient is seen holding the elbow with the elbow flexed, the shoulder dropped, and the head and neck flexed to the

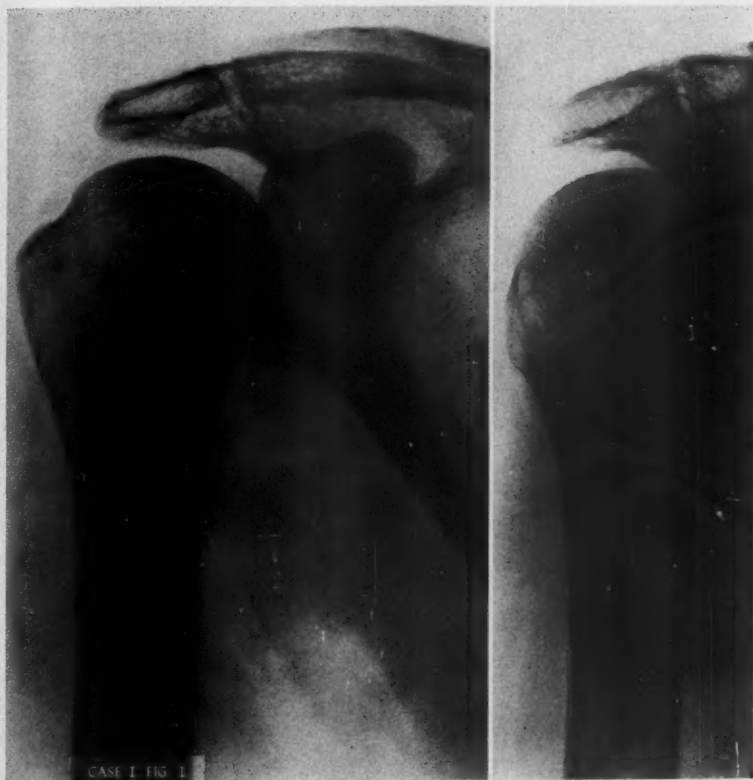


FIG. 1, Case 1. Small calcification in the subdeltoid bursa. Symptoms relieved with X-ray therapy.

affected side. Acute bursitis, with these signs and symptoms must be differentiated from a fractured clavicle or humerus. The patient usually gives a history of some annoying pain in the region of the shoulder for several months but not severe enough to consult a physician. Several hours or days following raising a window, lifting a child, or opening a door forcibly, severe pain and tenderness develops.

The severe localized tenderness, limitation of motion, and roentgenograms confirm the suspected diagnosis. Two, but better three, roentgenographic views



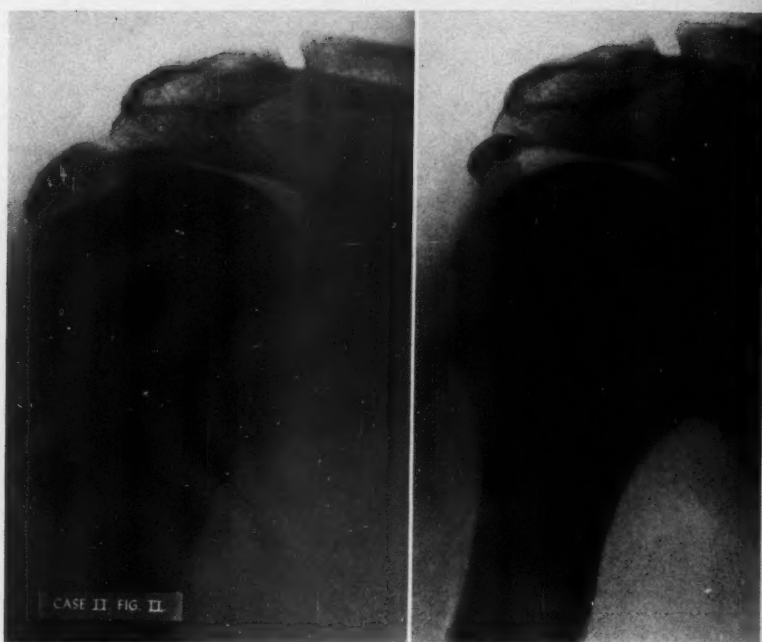


FIG. 2, Case 2. Large calcification in the bursa. Symptoms of long duration relieved with incision and curettage.



FIG. 3, Case 3. Small calcification in the bursa. Acute symptoms of short duration relieved with incision and curettage.

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of the shoulder should be taken if the patient's pain will permit. Roentgenograms with the shoulder in neutral, internal and external rotation will localize the calcification.

The severity of the patient's symptoms determines the type of treatment recommended. Local heat and diathermy may be used. Novocaine injection will usually give temporary relief. Injections of many different solutions have been recommended. Some patients have such acute pain that they will not permit injection of even novocaine. Others seem to have increased symptoms following injection of various solutions. I think that the chief value of the injection therapy is the needling of the bursa and rotator cuff. Novocaine does temporarily block the painful reflex. Injection therapy may give temporary relief but it does not promise permanent relief. Roentgenotherapy is a standard and recognized form of treatment for these conditions. But even my roentgenologist friends agree that it does not always give immediate and permanent relief.

Various discussions and articles on this subject usually end by stating that *even surgery may be indicated*. In over 150 patients having acute subdeltoid bursitis and tendinitis that I have operated upon, incision and curettage of the bursa and tendon has been the treatment of choice. The acutely suffering patient will want immediate and permanent relief. In my experience, surgery is the only means of securing this relief. After operation all patients received some immediate relief but were slow in recovering complete painless function of the shoulder. Most of them had complete painless function in one to four weeks. I have never seen a recurrence of the condition following incision and curettage.

The operation is simple. It should be done under pentothal or some form of general anesthesia. Through a 2 or 3 inch incision the entire bursa, musculo-tendinous cuff and long head of the biceps tendon can be explored. Following closure of the incision the shoulder may be passed through a full range of motion to free any adhesions that may be present. Also, following operation, the patient can and is encouraged to begin active motions. Very few of these patients required the service of a physical therapist in obtaining full painless motion.

#### CASE REPORTS

*Case 1.* Mr. W. C., a 60 year old salesman, was seen in November 1952. He had had pain in his shoulder a year previously and had been treated with roentgenotherapy in another city with relief. He was having recurrence of his symptoms and desired further roentgenotherapy. He was referred for such therapy after which his symptoms subsided (fig. 1).

*Case 2.* A 48 year old traveling salesman had had pain in his shoulder for two years. He was first seen on Aug. 9, 1952 at which time he was having severe pain and tenderness in his shoulder and would allow no motion. He had been treated for *arthritis* and had had *injections* and *medicines*. He had had all of his teeth removed and had received *chiropractic* treatments. He had taken large quantities of barbiturates. His shoulder was operated upon. A month later he had full range of motion with slight pain and was not taking barbiturates (fig. 2).

*Case 3.* Mrs. J. M. B., a 35 year old woman, was an active housewife and often engaged in active athletics such as swimming, golf, and tennis. She was seen on Oct. 27, 1952. She had been playing tennis the day before and that night had severe pain in her right shoulder. She was operated upon the next day and was back at her regular activities after one month (fig. 3).

# LABORATORY AND CLINICAL EVALUATION OF ANTRENYL, A NEW ANTICHOLINERGIC DRUG, AND ITS APPLICATION TO SURGERY

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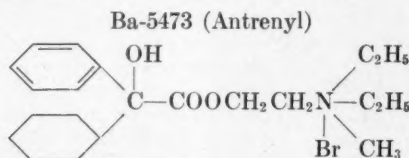
*Summit, N. J.*

The problem of epigastric pain is of prime importance to both the surgeon and the internist. The differentiation of upper abdominal pain is often difficult and perplexing. Of equal importance is the problem of treatment. During recent years much impetus has been given to the theory of autonomic imbalance as the cause of disease. In studying the effects of the predominance of one or the other divisions of the autonomic nervous system, considerable interest has been aroused in new autonomic effectors.

Anticholinergic drugs are perhaps the oldest of the autonomic effectors, and recent work has brought out a series of new cholinergic blocking agents. This work has re-emphasized the importance of the anticholinergic drugs both to the surgeon and to the internist. These new compounds are important in that they are more selective in their action, and this fact opens up new avenues of research. Because the parasympatholytic activity of a compound is potentially applicable to a great number of uses, the more selective the effect the greater the usefulness of the compound.

A series of trasentine analogues was studied for anti-ulcer properties and anti-gastric secretory properties in the Shay rat and in the Pavlov dog, Barrett and associates.<sup>2</sup> From these studies it was found that antrenyl\* (BA-5473) possessed a marked anticholinergic activity against certain vagal influences on the gastrointestinal tract. This compound has been intensively studied by several investigators, including Bein<sup>3</sup>, Plummer<sup>5</sup>, Bachrach<sup>1</sup>, and Mattman and Strutner.<sup>4</sup>

The following is the structural formula of antrenyl:



Antrenyl is a quaternary compound, stable in tablet and liquid form, and capable of being administered orally as well as parenterally.

Presented during the Louisville Assembly of The Southeastern Surgical Congress, Louisville, Ky., March 9-12, 1953.

\* Oxyphenonium bromide Ciba

This compound was tested on the Shay rat. The pylorus of the rat was ligated under anesthesia. Antrenyl was administered intravenously 15 minutes before the ligation of the pylorus, and at three and six hours after the pyloric ligation. The protective action of an anti-ulcer agent against the formation of rumenal ulcers in the Shay rat can be demonstrated by killing the animal 16 hours after ligation of the pylorus and comparing the size of the ulcers in the treated group with those found in the control group. Antrenyl was compared with atropine, diphenmethanil methylsulfate (prantal), and methantheline (banthine). The following photographs graphically illustrate the results obtained (figs. 1 to 5).

The almost complete protection afforded by antrenyl against rumenal ulceration in the Shay rat can clearly be seen in the accompanying photograph (fig. 2).

Antrenyl was next studied for its anti-gastric secretory properties, using as a test object the Pavlov dog. The results of some of the gastric secretory experiments are presented in figures 6 and 7. It will be noted that both the milliequivalents of free hydrochloric acid per 15 minutes and the volume of secretion for 15 minutes were significantly inhibited by antrenyl for the three hour test period.

Concomitant acute and chronic experiments revealed antrenyl to be a safe compound used in laboratory animals. Laboratory workers next studied the effect of the drug on themselves and found it to be free from marked side effects when taken in doses which were later found to be within or even above therapeutic requirements, Barrett and associates<sup>2</sup>, Plummer and associates<sup>5</sup>.

#### ANALYSIS OF CLINICAL RESULTS

From the foregoing charts, one can see the possibilities of using antrenyl as a vagal blocking agent in clinical medicine because of its pronounced anticholinergic effects. It was therefore decided to test the drug on patients with peptic ulcer since their syndrome is essentially that of predominance of cholinergic activity. The method of study devised was as follows: (1) an upper gastrointestinal roentgenographic series was completed to establish the diagnosis; (2) medication with antrenyl was begun, and three weeks later a repeat roentgenogram was taken; (3) a third roentgenogram was taken at the end of three months. In addition, gastric analysis was made in a few patients before and after administration of antrenyl. Roentgenographic findings were correlated with clinical symptoms.

In analyzing the results after using antrenyl, the patients were divided into three groups. The first and largest group consisted of those patients with classic symptoms of peptic ulcer and with an ulcer crater demonstrable by roentgenogram. The second group were those with typical clinical symptoms who had indirect evidence (spasm, tenderness, and deformity of the duodenal bulb) of peptic ulcer by roentgenogram, but in whom the actual crater could not be visualized. The third group included those patients who did not return for treatment and whose follow-ups were therefore irregular.

The following charts give the results in 54 cases of peptic ulcer studied in this series (figs. 8, 9, 10).

All patients were ambulatory, and antrenyl was begun in doses of 5 mg. before

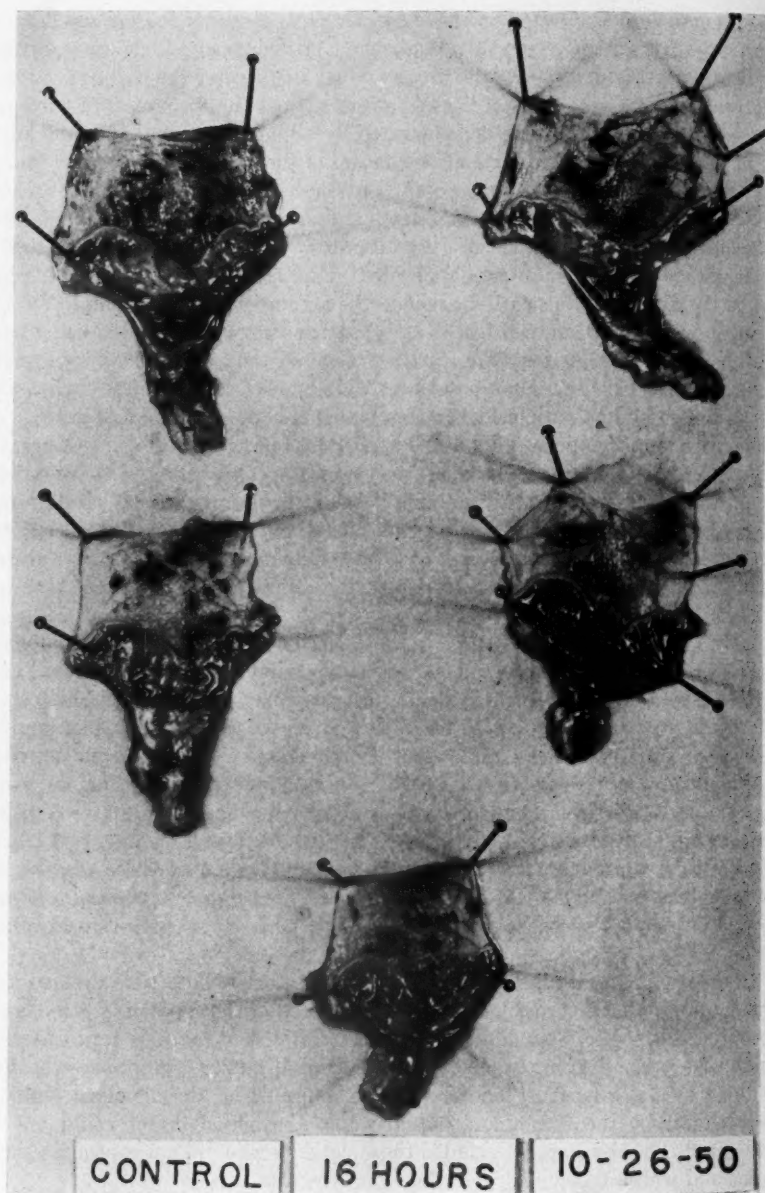


FIG. 1

meals and at bedtime, and increased as necessary to achieve the desired effect. None complained of bitter taste, and the only side effects noticed were mild dryness of the mouth and some constipation. Approximately half of the patients

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had been receiving banthine, and by comparison they stated their side effects were less marked with antrenyl. It was not necessary to stop the medication in

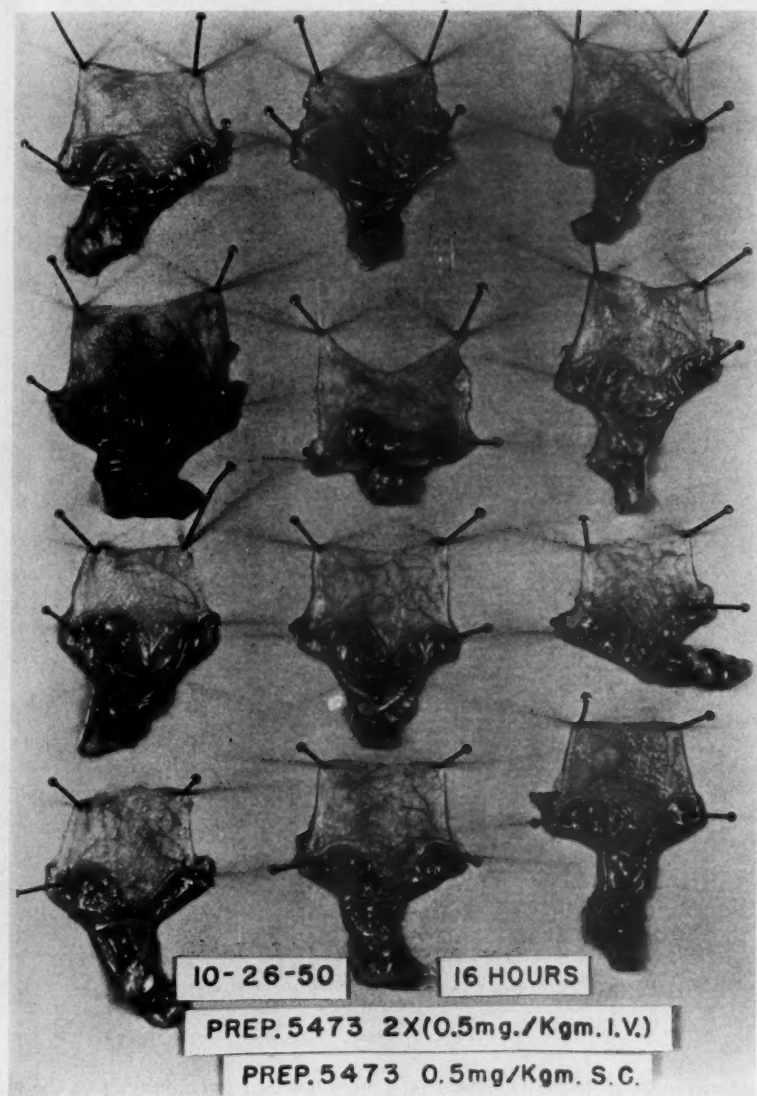


FIG. 2

any case because of untoward reactions. Because we wished to test the primary efficacy of the drug the patients were not given a specific dietary regime. In nearly every case pain began to decrease immediately and had practically dis-

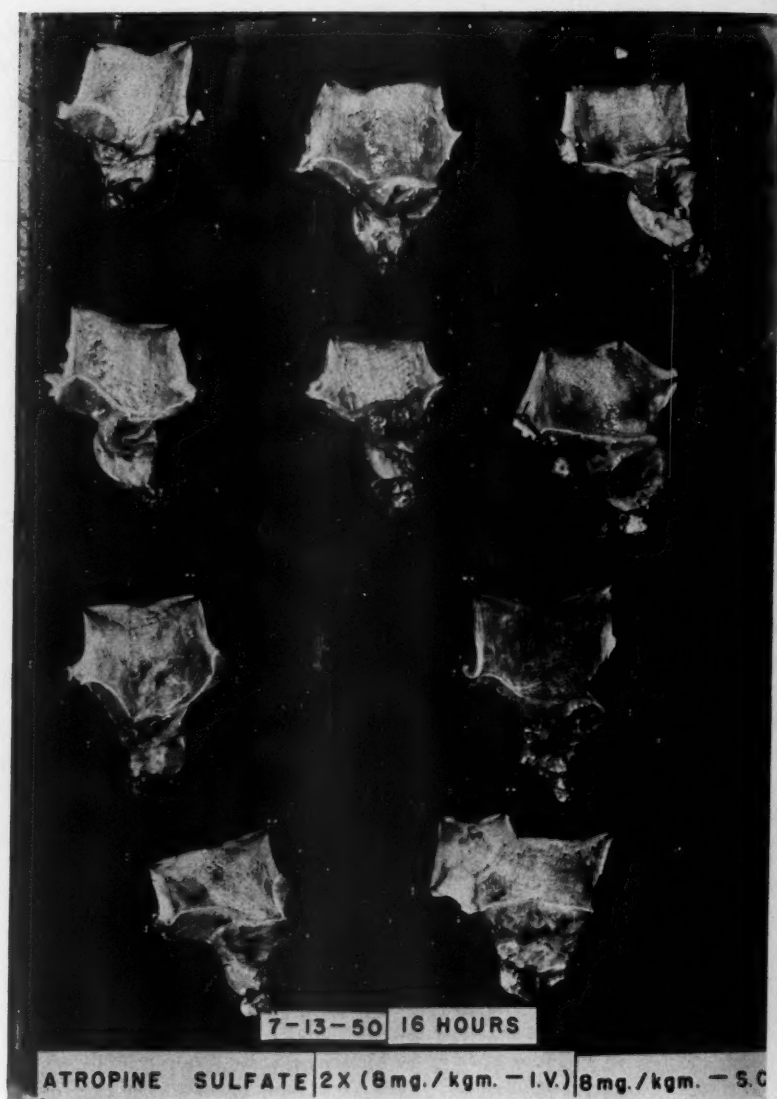


FIG. 3

appeared in 24 to 48 hours. However, a very few had some pain up to one week before complete relief was obtained. It was interesting to note the change in the personalities of the individuals as symptomatic control was achieved in that they seemed to live more nearly normal lives without feeling that they were ulcer invalids.

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As a long-term follow-up on these cases, which extended from 3 to 18 months, 1 patient had a gastro-enterostomy due to pyloric obstruction as a result of healing of his ulcer; and another patient had a partial gastric resection after discontinuing his medication and developing pyloric channel edema and ulcera-

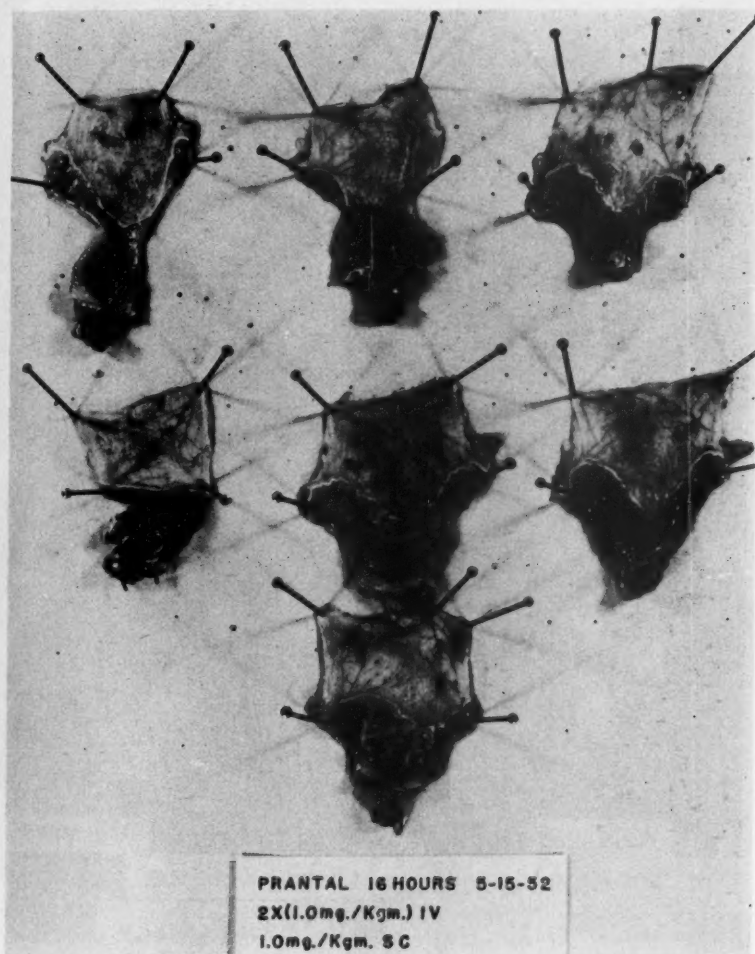


FIG. 4

tion. These 2 cases, with 1 case of complete failure, total 3 surgical cases out of 54. There were a few patients who, after being off their medication for a few months, had a return of symptoms, usually after dietary or alcoholic over indulgence. However, after resuming their medication for a few days cessation of symptoms resulted.

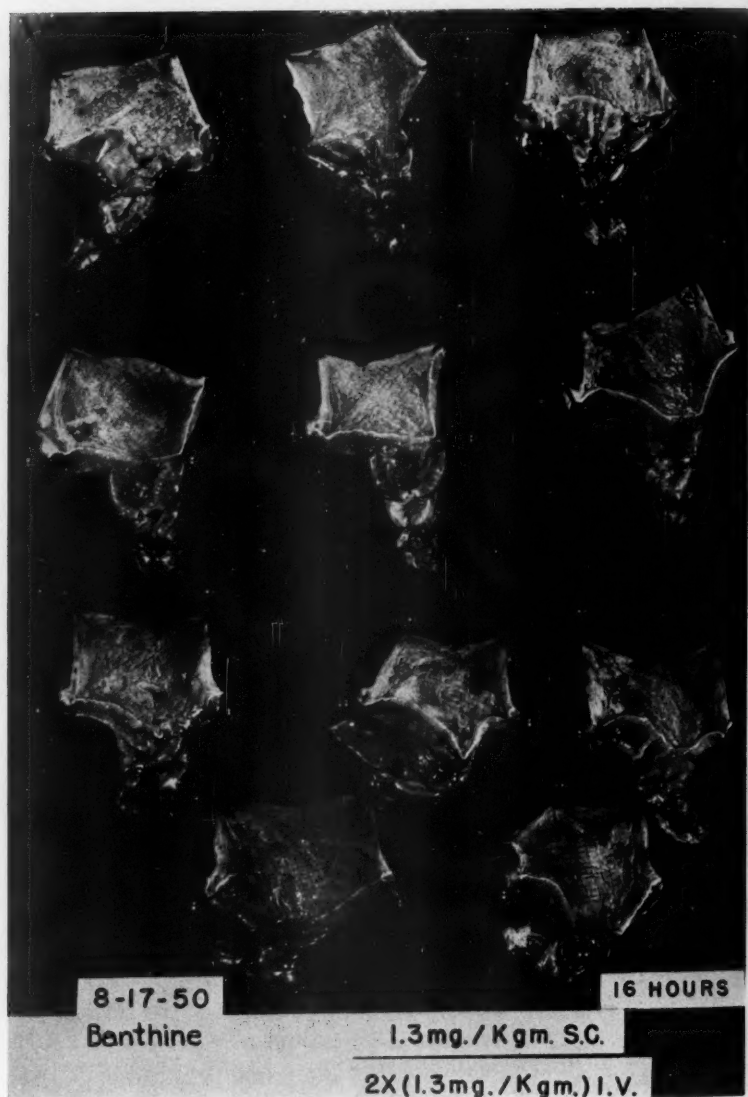


FIG. 5

It is believed that some patients should continue their medication indefinitely due to their personality and psychic make-ups. There are others who will probably have to take their medication only during the spring and fall, the ulcer seasons, while still others may be able to control their ulcers by modification of their living habits and may not require further treatment.

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## ADDITIONAL USES OF ANTRENYL

Approximately 35 patients in whom the roentgenographic report was that of hypertrophic gastritis without ulcer were treated with antrenyl on an average dose of 5 mg. four times daily. Results have been uniformly good with decrease of pain, epigastric burning, and gaseous eructation.

## SUPPRESSION OF GASTRIC SECRETION

Pavlov Dog - Drugs Admin. Orally

Average Volume of Gastric Secretion/15 min.

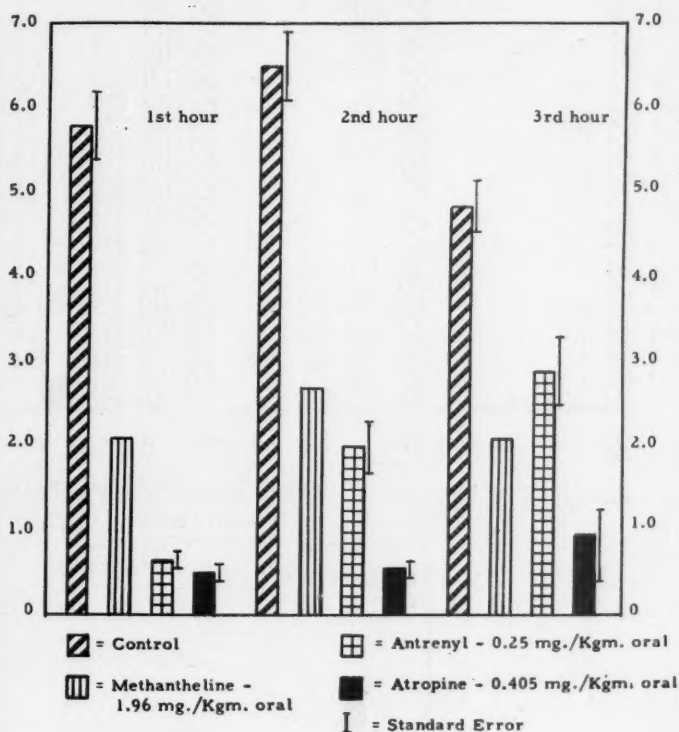


FIG. 6

On the basis of the foregoing experience, proving the marked anticholinergic effects of antrenyl, work is now being expanded for its surgical use. The writers have come to the conclusion that, since gastric resection is not the answer in all cases of peptic ulcer, patients should not be subjected to partial gastric resection until they have been given an adequate trial on antrenyl. In addition, antrenyl is probably an ideal agent to use in cases of acute hemorrhage from peptic ulcer in order to slow gastric motility and decrease the hemorrhage. Furthermore, in



## SUPPRESSION OF GASTRIC SECRETION

Pavlov Dog - Drugs Admin. Orally

Average Milliequivalents Free HCl/15 min.

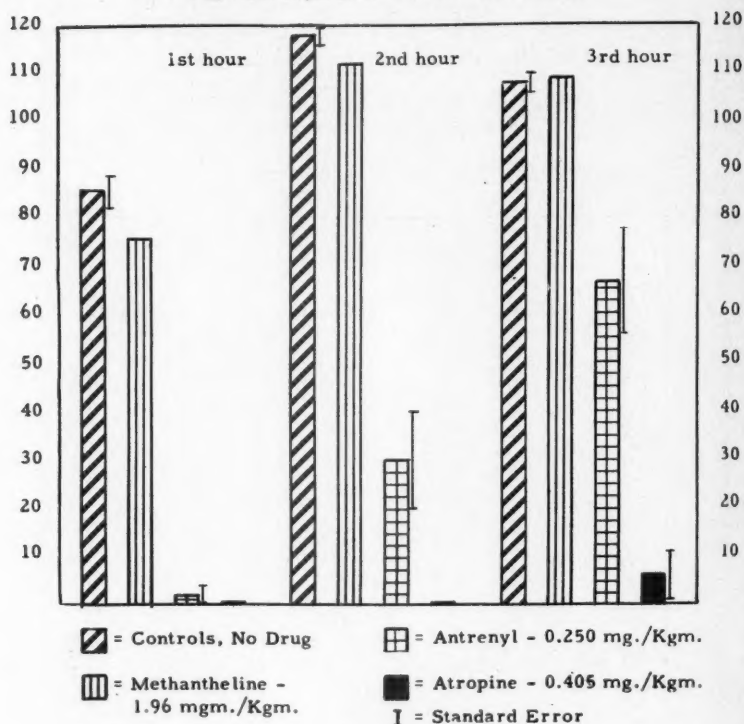
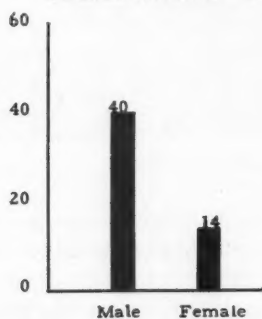


FIG. 7

TOTAL PATIENTS - 54



Age Range . . . . . 26 yrs. - 89 yrs.  
 Duration of Ulcer Symptoms - 1 mo. - 25 yrs.  
 Average duration of Symptoms - 6 yrs.  
 Average Dosage of ANTRENYL- 10 mgm. q.i.d.

FIG. 8

those cases which are to be subjected to partial resection, an anastomosis can be more accurately made if antrenyl is used preoperatively to lessen the hypertrophic gastritis, which is always present; and to reduce the disproportion between gastric and jejunal mucosa. Also in preparation for surgery for hiatus hernia, antrenyl can produce a marked degree of esophageal and gastric relaxation.

*Results of treatment with antrenyl in peptic ulcer patients proven by X-ray*

	Pts. No.	Healed				Not Healed	Follow-up
		3 Wks.		3 Mos.		3 Mos.	
		No.	%	No.	%	No.	
Group I							
Ulcer with crater by X-ray.	27	23	85.1	25	93.3	2	1. Dosage increased—healed in 2 wks. 2. Complete failure. Subtotal gastrectomy done. Pre-CA finding.
Group II							
Ulcer symptoms with indirect X-ray evidence.	7	6	85.7	5	71.4	2	1. Healed after increasing dosage. 2. Took only 5 mgm., and not regularly.

FIG. 9

GROUP III

*Definition:* Patients with peptic ulcer who did not have regular follow-up schedule.

*Diagnosis:* 13 patients—active crater demonstrated.  
7 patients—indirect evidence of ulcer.

*Total:* 20

Result of X-rays at last visit:

No. Healed 18  
Pet Healed 94.5%  
Not Healed 1 (only took 5 mgm. q.i.d.)

FIG. 10

Antrenyl likewise has a definite place in relieving the *spastic pain* of acute pancreatitis, and biliary and renal colic.

Reports from Stephen and co-workers<sup>6</sup> of the Department of Anesthesiology, Duke University School of Medicine, point out that antrenyl has been used (in place of atropine) as preanesthetic medication in about 350 patients, and their impression so far is that it is superior to atropine and banthine in this respect in the commonly used doses. They emphasize that a series of 2,000 or

3,000 cases will be required to arrive at definite conclusions, and they are now embarked upon such a series together with animal studies.

The drying effects of antrenyl in 1 mg. doses given intravenously are excellent. Further investigation is more particularly aimed at proving what vagal blocking effects can be expected with reasonable consistency in human beings.

The group at Duke University has found that 1 mg. given intravenously will correct the bradycardia and hypotension associated with marked vagal stimulation as it may occur during operation. In the limited series observed to date they find that this effect is immediate and appears to persist for the duration of the surgical procedure.

Postoperatively antrenyl has been efficacious in relieving nausea and vomiting as well as functional pylorospasm.

#### SUMMARY

The pharmacology and chemistry of a new anticholinergic agent have been presented. The results in 54 cases of peptic ulcer show the drug to have great promise in the regime of treatment of parasympathetic predominance. In addition, the surgical uses of this preparation are numerous and the drug should prove to be of vital importance in the hands of the general surgeon. These surgical uses may be listed as follows:

1. To more clearly define cases of peptic ulcer for surgical intervention.
2. To decrease gastric motility in cases of hemorrhage from peptic ulcers.
3. In the preoperative management of patients for gastric resection to lessen hypertrophic gastritis.
4. To lessen pain in acute pancreatitis.
5. To relieve biliary and renal colic.
6. To relieve postoperative nausea due to pylorospasm and vagal overactivity.
7. As a preanesthetic medication.

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## EDITORIAL

### SURGEONS AND NEUROSES

A high percentage of people who consult physicians are victims of neuroses of various types. Many people suffer symptoms purely of psychic origin simulating actual disease. Further, patients with actual disease frequently have concomitant psychoneuroses. Weiss and English,<sup>1</sup> combining the observations of internist and psychiatrist, divide their patients into three groups:

1. One-third "*do not have any definite disease to account for their illness . . . psychosomatic medicine is chiefly concerned with these.*"
2. "Approximately *another third* of the patients who consult a physician have symptoms that are *in part dependent upon emotional factors.*"
3. Another third "*composes a group of disorders generally considered wholly within the realm of 'physical disease'.*"

There is no lack of enlightening literature devoted to the neuroses and kindred ailments, but unfortunately most of it has been written for the psychiatrists. Medical students, general practitioners, internists and surgeons have been neglected in this regard and left uninformed. It is time that the teachers of psychiatry descend from their thrones to give medical students comprehensive practical courses in the management of neuroses, and produce literature at the same level for the guidance of practitioners who first see psychogenic patients and are the logical ones to supervise treatment. Surgeons (i.e., *men who operate*) belong in this class of the uninstructed.

Modern, improved diagnosis has made surgery more effective. Surgical death rates and postoperative morbidity have diminished more rapidly during the last 20 years than during any other equal period. In spite of these salutary achievements, the surgeon's job is unfinished. His next endeavor should be devoted to removing a black spot on his record—the stigma resulting from unnecessary operations. We know, and the public knows, that much unnecessary surgery has been done and is now being done. How is this to be corrected? By realizing that every case, where the pathologic reasons for operating are not clearly defined, should have a personality study before instituting treatment. Usually the surgeon is *too busy* or thinks psychology is beyond his province. If he has well qualified internists in his organization, they may be able to make the study for him. In the absence of such help, it is up to the surgeon himself. It is time he learned how to make personality studies. Instructive literature is lacking. A simple plan that has proved effective is here suggested.

Assign one hour for the study. More time or later appointments are rarely necessary. Do not tell the patient that your time is limited, as she may get the idea that you are in a hurry, and that will interfere with her thinking. Instruct your office force that you are not to be interrupted. Sit down. The seat of your pants is one of your most valuable professional possessions, and, when used, inspires the patient with the feeling that you are not in a rush and are personally interested. Don't use a history sheet. Concentrate on the talk. Tell the patient

that the careful, detailed diagnostic methods previously used have not entirely solved her problem; that more information is necessary before arriving at a diagnosis and recommending treatment. Then comes your systematic inquiry.

*A happy childhood makes for nervous stability.* Many adult neuroses originate early, and therefore a behavior and environmental history of childhood is necessary. Let the patient do the talking, with a guiding comment now and then to keep her on the right track. It is usually not difficult to get a clear over-all picture of a patient's younger years. Parental conduct has a lifetime influence on a child's happiness and emotional life. Were the patient's parents sympathetic with each other and their children? Were they quarrelsome; given to anger; at cross purposes in child discipline; too strict; too coddling? Did they nag about school grades? Did they welcome their children's schoolmates in the home? Did they cooperate and show that they trusted their daughter when she had *dates*? Did your patient have *tantrums* in resistance to parental discipline? Etc., etc.

During school days teachers partially replace parents. They may have the same virtues as parents, and the same faults, thus accounting for their influence, good or bad, on a child's nervous system. It is necessary to know your patient's normal or abnormal conduct in relation to her teachers and schoolmates.

Inquiry into adult neuroses is conducted according to a definite plan: "How do you live on your 24 hours a day?" Thus the patient is guided into giving a full day's record of her life. What kind of house does she live in? Do modern appliances make work easier? How many hours a day devoted to housework? Is there time for rest; for intramural and extramural social activities? What are her adjustments thereto; or to in-laws butting in; husband's behavior; economic status; jobs in addition to domestic duties; sexual habits; contraceptive methods; behavior of her children? How about vacations; club memberships, and church responsibilities?

At the termination of the inquiry the surgeon's job really begins. If he has an understanding of his patient's psychology, he is prepared to treat any organic disease that may be present, and, in addition, correct his patient's emotional symptoms, not with medicine but with wise advice. If he has had broad experience and is sympathetic, he can do much to improve his patient's distorted thinking by analyzing each of the several neuroses present; showing how they may be minimized or eliminated with assurance of ultimate improvement or recovery. Follow-up office visits or correspondence with out-of-town patients will effectively supplement the treatment.

One of the largest groups of neglected patients is made up of women who have been operated upon. A surgeon usually makes rounds rather hurriedly and discharges his patient while he is on his feet. That is poor technic. Most women have a lot of worries that have been bothering them and can't bring themselves to ask questions of a man in a hurry. That can be easily corrected. A couple of days before contemplated discharge from the hospital, tell the patient to get a big piece of paper and a pencil, and put down and number all the questions regarding her health that have disturbed her. The average number of questions is 15. When the surgeon is ready to send the patient home, he should sit down



with the list in hand and discuss each of the items enumerated. They can usually be disposed of to the satisfaction of the patient. He should give specific instructions regarding domestic work, sex life, and driving automobiles. Cancerphobia must be firmly removed. A surgeon's job, however skillful his operating, is not complete until he has set his patient's mind at rest.

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University of Utah, Salt Lake City*

RALPH T. RICHARDS, M.D.

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## EDITORIAL

### ANATOMY, PHYSIOLOGY AND TECHNICAL CONSIDERATIONS IN INGUINAL HERNIA

Studies in the operating room of the inguinal region in the presence of hernia have brought to light much information that was not evident in cadaver dissections and have advanced interesting speculations relative to unknown factors that remain to be investigated.

Technical problems related to inguinal hernia have long been concerned with the repair of the defect in anatomy. In the instance of indirect hernia the defect has been ignored. The lack of good results following repair of indirect hernia has been reflected in the numerous variations that have been devised from the classical operations of Bassini, Ferguson and Halsted. It appeared feasible to reinvestigate some fundamental problems at a clinical level.

A veritable babel of tongues has stemmed from the use of inaccurate terminology so that the student has been utterly confused when the anatomy at operation has not conformed to a picture in the anatomy book. Clarification of the problem of inguinal hernia must begin with an accurate terminology, particularly by the surgeon in the operating room.

The neophyte has been confused by the frequent variations in the tissue layers, a condition not sufficiently stressed during his training. Few individuals present anatomical layers at the operating table that coincide with drawings and colored illustrations in our text books and leading articles. Correction of this situation is exceedingly important. Variations in the tissue planes have been due to habitus, congenital defects, senile changes and the trauma incident to hernia. These variations must be evaluated on a clinical basis alone. Doctor C. I. Owen, pathologist at Grace Hospital, has examined microscopically the focal tissues in 100 cases and was unable to demonstrate any relationship between the presence of hernia, the state of the tissue and the patient's age.

Sir Arthur Kieth first described the physiology of the inguinal region in the operating room. This important work revealed that the mechanics of the inguinal region were not limited to the canal area but included the internal hiatus area, both acting as a single unit (inguinal shutter). We believed that the stresses set up by the internal oblique muscle upon the anchored inguinal canal region was an important factor in recurrence.

Variations in the strength of the several tissue layers were frequent findings. Estimation of this condition was possible only on a clinical basis and required much practical experience. It appeared pertinent to take the stand that when the tissues were too poor in substance to withstand the assaults of the patient's activities that any repair, regardless of the skill of the surgeon, was not sufficient to insure against recurrence. Local reinforcement by means of a patch was surely indicated in these patients.

Our approach to the repair of inguinal hernia has been based upon three problems. The first problem was concerned with the discovery of any of the many

possible defects through adequate exposure and restoration of the basic anatomy. Among the ancillary procedures was the separate closure of all apertures due to direct hernia anywhere along the semilunar line, restoration of the inguinal floor, the freeing of the attachments of the various sacs and removal of lipomas from the internal hiatus. The second problem involved elimination of the stress factor incident to the normal physiology by completely anchoring the inguinal shutter, a procedure that should be common to the treatment of all inguinal hernias. The third problem was concerned with the reinforcement of deficient tissue layers by means of full thickness skin grafts, tantalum gauze mesh or other substances.

EARL G. M. KRIEG, M.D.  
Detroit, Mich.

## BOOK REVIEWS

The Editors of *The American Surgeon* will at all times welcome new books in the field of surgery and will acknowledge their receipt in these pages. The editors do not, however, agree to review all books that have been submitted without solicitation.

*Functional Neuroanatomy.* By WENDELL J. S. KRIEG, B.S. in Med., Ph.D. Professor of Anatomy; Formerly Professor of Neurology and Director of the Institute of Neurology, Northwestern University Medical School. The Blakiston Company. Second Edition. Cloth, 659 pages. \$9.00.

The second edition of this excellent neuroanatomy follows the general format of the first edition. It is one of the few textbooks which presents neuroanatomy from a functional point of view, correlating anatomical detail with clinical function. Logical development of the material, clear text, and the author's own superb illustrations and three dimensional phantoms make for interest, readability, and easy retention. The consideration of the brain stem segments in functional units illustrates these points. It is gratifying to see that a large part of the work is devoted to the increasingly important cerebral cortex, thalamus, and hypothalamus, areas too often neglected in the usual neuroanatomical presentation.

The text has been brought up to date. In place of the usual bibliography, the author lists the classic works on each subject and adds a list of current periodicals germane to neuroanatomy.

This presentation of functional neuroanatomy is believed to be the best textbook currently available to the student in this field and is highly recommended to the medical student, neurologist, and surgeon interested in neurology.

CHARLES E. BRACKETT, JR., M.D.

*Physical Examination of the Surgical Patient.* By J. ENGLEBERT DUNPHY, M.D., F.A.C.S., Associate Clinical Professor of Surgery, Harvard Medical School; Surgeon, Peter Bent Brigham Hospital; Consultant in Surgery, Children's Medical Center. And THOMAS W. BOTSFORD, M.D., F.A.C.S., Clinical Associate in Surgery, Harvard Medical School; Senior Associate in Surgery, Peter Bent Brigham Hospital; Associate in Surgery, Children's Medical Center. Philadelphia and London, W. B. Saunders Company, 1953. \$7.50.

In the preface of this book of 300 pages, the authors state that "an x-ray or a laboratory test is so easy to order, or a consultation is so readily available, and the results of either or both often appear so definite that the art of simply 'looking at the patient' is in danger of being lost." This book teaches surgical diagnosis made with the "Tools: eyes, ears, fingers, nose and brain." There is nothing that needs more emphasis in surgical diagnosis today.

This book tells you how to examine a patient from the head to the feet to determine the presence or absence of disease or abnormality. The technic is described clearly. The illustrations are many and good. Anatomy in relation to diseased organs is here depicted. The beginner will learn the terminology of surgical diseases. There are little *tricks* about making an adequate physical examination that every clinician must learn. They are found in this text.

This book is needed by every medical student and hospital resident. A copy should be on the desk of every teacher of surgery, not only as an outline for thorough teaching of physical diagnosis in surgery, but to act as a constant check on his methods of teaching lest they wander from real physical diagnosis to the frequently easier and less time-consuming diagnosis of the laboratory. The general practitioner would greatly profit by reading this book as a refresher course in surgical diagnosis.

Certain things contained in this volume have impressed the reviewer. They are: (1) The

foreword by Dr. Francis D. Moore which tells in precise language the objective of the book; (2) the emphasis that physical diagnosis must be made by the natural senses; (3) the considerate treatment of the patient during examination; (4) the logical sequence of the surgical subjects presented; (5) and finally, the affectionate dedication of the book to two well-known masters in the art of teaching surgery, Doctor David Cheever and Doctor John Homans.

THOMAS G. ORR, M.D.

*Trichlorethylene Anaesthesia.* By GORDON OSTLER, M.A., M.B., B. Chir. (Camb.), D.A., Deputy First Assistant, Nuffield Department of Anaesthetics, University of Oxford; Formerly Research Assistant, Nuffield Department of Anaesthetics; Senior Resident Anaesthetist Hill End (St. Bartholomew's) Hospital; Assistant Editor, *British Medical Journal*. Edinburgh and London, E. & S. Livingstone Ltd.; Baltimore, Maryland, The Williams and Wilkins Company, 1953. \$2.25.

This short monograph on trichlorethylene anesthesia is very timely because of the high pressure tactics used by certain pharmaceutical houses to obtain widespread distribution of the agent. The author presents in a factual manner the *pro's* and *con's* of the agent without bias. All of the chapters are brief and to the point, leaving nothing for speculation. The author emphasizes the dangers following the indiscriminate use of the agent. The author's literary style is typically British, and grammatically perfect. References are numerous and are placed at the end of each chapter. The monograph is recommended reading for all those interested in and using trichlorethylene. The general practitioner should read this monograph before using trichlorethylene.

PAUL H. LORHAN, M.D.

*Local Analgesia: Abdominal Surgery.* By R. R. MACINTOSH, M.A., D.M., F.R.C.S. (Edin.), D.A., M.D. (hon. causa), Buenos Aires, Nuffield Professor of Anaesthetics, University of Oxford, Civilian Consultant in Anaesthetics, Royal Air Force; Examiner for the D.A.; Anaesthetist, United Oxford Hospitals. And R. BRYCE-SMITH, M.A., B.M., B.Ch., D.A., First Assistant, Nuffield Department of Anaesthetics, University of Oxford; Anaesthetist, United Oxford Hospitals, At present on leave as Assistant Professor of Anaesthesia, Western Reserve University, Cleveland, Ohio. Edinburgh and London, E. & S. Livingstone Ltd.; Baltimore, Maryland, The Williams and Wilkins Company, 1953. \$5.00.

This monograph is excellently written and is typically *Oxfordian*. The publishers have gone to a great deal of expense in presenting this monograph, especially in duplicating the drawings so excellently. To obtain the maximum information from this monograph it is recommended that the student carefully study the drawings. These are in color and excellently and clearly demonstrate the relationship of the various structures.

Though it is primarily intended for the anesthesiologist, surgeons will find the monograph of interest in helping them review their neuroanatomy.

PAUL H. LORHAN, M.D.

*An Atlas of Surgical Exposures of the Extremities.* By SAM W. BANKS, M.D., Associate Professor of Orthopedic Surgery, Northwestern University Medical School. And HAROLD LAUFMAN, M.D., Associate Professor of Surgery and Director of Experimental Surgery, Northwestern University Medical School. First Edition, 379 pages with 552 illustrations. Philadelphia, W. B. Saunders Company.

This Atlas consists of 179 carefully drawn plates illustrating step by step the anatomical structures encountered in the various incisions used in operations on the extremities. Facing each plate is a listing of indications for the use of the illustrated incision as well as a brief annotated description of the anatomical structures and relationships as they develop from the skin incision to full exposure of the operative site. The illustrations were made from photographs taken during dissections on cadavers and are superb in clarity and simplicity. This volume should be very useful to students and residents in General Surgery, Neurosurgery and Orthopedic Surgery and will serve as a timely *refresher* to the experienced surgeon who operates on the extremities only occasionally.

GEORGE HIGGINS, M.D.



Books received are acknowledged in this section, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

*Thoracic Surgical Management.* By J. R. BELCHER, M.S., F.R.C.S., Consultant Surgeon at the London Chest Hospital, Late R.S.O. at the Brompton Hospital, London. And I. W. B. GRANT, M.B., M.R.C.P. (Edin.), Assistant Physician, Edinburgh Northern Hospitals, Royal Victoria and associated Hospitals, Late R.S.O. at the Brompton Hospital, London. With a foreword by SIR CLEMENT PRICE THOMAS, K.C.V.O., F.R.C.S., Surgeon to Westminster and the Brompton Hospitals, London; Consulting Surgeon, King Edward VII Sanatorium, Midhurst. London, Baillere, Tindall and Cox; Baltimore, Maryland, The Williams and Wilkins Company, 1953. \$3.50.

*Morris' Human Anatomy.* Eleventh Edition. Edited by J. PARSONS SCHAEFFER, A.M., M.D., Ph.D., Sc.D., D.Litt., Professor of Anatomy and Director of The Daniel Baugh Institute of Anatomy, Emeritus, The Jefferson Medical College. New York and Toronto, The Blakiston Company, 1953. \$16.00.

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